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By Sir ROBERT MUIR, M.D. Edin., F.R.C.P. Lond. & Edin., LL.D., F.R.S.
PROFESSOR OF PATHOLOGY IN THE UNIVERSITY OF GLASGOW

MAY I ask your indulgence if at the outset of my address I refer to a matter which has doubtless presented itself to the minds of you all—the break with precedent which has admitted to the high honour of the Lister award one who is not himself a surgeon? I come before you as in some sort a layman, with a layman's disabilities, but I am fully conscious that in your catholicity of outlook your desire has been to stress the fact that pathology and bacteriology were the base and the essential condition of Lister's work in surgery. I appreciate to the full the signal distinction which has been conferred upon me.

On the occasion of the 109th anniversary of Lord Lister's birth, we are met to do honour once more to his memory. In fulfilling my obligation to give a lecture I should have liked to make the subject Lister's scientific work, but a short time ago I gave an address on this subject to the Canadian Medical Association, and I felt that it would not be justifiable to offer on the present occasion what would necessarily be a repetition in great part of what I had already said. I have had perforce to choose another subject. Before speaking on it I should like to offer a few remarks of a general kind.

Than the life work of Joseph Lister there is in the history of our profession no better example of the truth that advance in practice can come only from increase of knowledge, hardly won by continuous and painstaking investigation. The scientific achievements of the earlier part of Lister's life are naturally overshadowed by his epoch-making contributions to surgery in the latter part, but no one can appreciate how his immortal benefaction to mankind was bestowed without following the steps in his scientific progress. And it is to his earlier years that we must look for a just estimate of his gifts as an investigator. "Science for its own sake" might be said to have been his motto at first, but this was modified as practical requirements arose.

By the time he had gone to Glasgow at the age of 33 he had published more than a dozen papers on subjects histological, physiological, and pathological, several being historical landmarks. In them is apparent that combination of detailed observation and breadth of outlook which marks the master mind. While occupied with minutiæ he was ever seeing afar and thinking broadly. He lived both in valleys and on the heights. And if we bear in mind the simplicity of the apparatus at his disposal and also the fact that his investigations were made in the spare time of a busy life, we cannot but marvel at his recorded achievements. Is there anything more pleasing or instructive in the history of research than the picture presented in his biography by Sir Rickman Godlee—the picture of Lister after a day's work was over carrying on his experiments till the early morning hours, spending what he called "a glorious night" in the study of the phenomena of inflammation?

The year 1865 was the turning-point in Lister's life for he then saw the bearing of Pasteur's researches; the fundamental facts regarding fermentation and putrefaction thereafter occupied his thoughts. A principle was grasped by him for the first time and his task then became an endless series of experimental trials, yet a sure evolution towards its successful application. In this his powers and methods to which I have referred are again clearly in evidence. The tale has often been told and is known to you all. In his opening lecture when he went to the chair of clinical surgery in Edinburgh in 1869 he was able to use these words, with confidence yet with modesty, "The germ theory is the pole-star which will guide you safely through what would be otherwise a navigation of hopeless difficulty." It is to me a pleasing thought that after having practically completed his work on antiseptics and having bestowed on mankind the greatest gift it has received, he should have been able once more to follow his bent and devote himself with unabating zeal to more purely scientific problems. His classical paper "On the lactic acid fermentation and its bearings on pathology" is a remarkable example of the outcome. Lister indeed possessed the essential qualities of the ideal investigator.

I close with the words which ended my previous address.

"In Lister's own time there were those who followed him along his way with understanding, expectancy and generous pride. There were those too who knew no more than to accord him a grudging kind of honourable mention when they ought to have sat at his feet. In these our own days, there can be but one attitude, that of veneration, and our veneration goes forth with a personal intensity to the man whose encompassing kindness made all humanity his concern. In him rare gifts and rare goodness met and greeted each other, made a pact of mercy and kept it. In commemorating once more the consecrated work of Joseph Lister we salute the memory of a man great in intellect and in soul, great in aim and achievement, great and humble in triumph."

* * *

In speaking on malignancy I shall keep to very general terms. It would be impossible to discuss the various views with regard to the nature and origin of malignant tumours, and it is not my object to do so. I shall rather state as simply as I can how the subject presents itself to me after a relatively long life as a pathologist. What I have to say falls mainly into three parts. In the first place, I shall speak of our present knowledge of the characters and ætiology of malignancy, as the result of observation and experiment; in the second place, I shall illustrate some of the chief points by my own observations on malignant disease of the mamma; and lastly, I shall briefly consider the essential nature of malignancy.

Some Features of Malignancy

I have used the term "malignancy" in my title rather than "neoplasia" since it may be taken to indicate the latter in its extreme deviation from normal growth. This entails the disadvantage that simple tumours and the graduated series of growths which may originate from one tissue are not considered, but I do not think the discussion will be seriously affected thereby.

It is unnecessary here to detail the nature of malignancy. In a general way malignancy may be regarded as an abnormal behaviour of cells, consisting

* The Lister memorial lecture for 1936, delivered before the Royal College of Surgeons of England on April 7th.

essentially in uncontrolled growth. It is evidenced by deviations in cell structure, dedifferentiation or anaplasia and sometimes extreme aberration in type, and it is often characterised by metabolic changes, especially in respiratory functions. But these and other properties are merely indications of changes in the biology of the cells, and do not in any way explain these changes; in other words, they are evidences of altered behaviour. It has been pointed out by others that normal cells will proliferate indefinitely if the conditions are favourable; this is seen in tissue cultures where the cells are free from adjacent tissues. Such cells, however, on being reintroduced into the body are once more restrained by the tissue tension which they encounter. Malignant proliferation, on the other hand, overcomes the controlling influence of the surrounding tissues and continues indefinitely in spite of it; this is most satisfactorily studied in the case of carcinoma. The term "autonomous" is eminently suitable as it implies that the malignant cells are a law to themselves. They invade and destroy the tissues while the latter exert their powers of restraint and are sometimes successful. But the proliferation must not be regarded as all-powerful. Experimental work on transplantation of tumours shows that the margin between growth and non-growth is comparatively narrow, and observation on malignant disease in the human subject supplies numerous examples of malignant cells being overcome and disappearing locally. The actual malignancy is in fact the surplus malignancy against tissue resistance.

While malignant cells are frequently overcome locally by stroma reaction, there is, however, no satisfactory evidence that weakened resistance of connective tissue will in itself lead to malignancy in the related epithelium; although *diminished tissue tension* has been put forward as a factor by various writers. As I have said, we are dealing with a biological change in the cells which is not brought about in this way. Furthermore, the malignant character once acquired seems to be a permanent property of the cells; they may be destroyed or die out, but they do not, so far as we know, regain a normal behaviour. Thus tumours have been transplanted in mice over many years without loss of malignancy. Likewise, tumour cells after having been grown in cultures separate from the other tissues for a time manifest their properties again on introduction into a living animal. I wish to emphasise here that the biological properties of the cells appear to have undergone an essential alteration which is apparently transmitted to their descendants.

With regard to *congenital abnormalities* in relation to malignancy I cannot speak in detail. These are not infrequently the bases of malignant growth—without the abnormality the tumour would not have arisen. Undoubtedly, too, the liability to malignancy varies in different examples of such abnormalities; compare, for example, the high incidence of malignancy in teratoma testis with that in pigmented nævi. Not many nævi originate a malignant melanoma. The incidence of malignancy must be investigated in the case of each abnormality. It is possible that abrogation of function arising from displacement of cells brings with it an increased tendency to malignant proliferation but, as I have said elsewhere, embryonic cells, though energetic in proliferation, are just as much under the laws of controlled growth as those of the adult tissues. And we have clear evidence that in the origin of malignancy in congenital abnormalities irritants and cell stimuli play a part just as in the case of normal tissues. Undoubtedly the most striking examples of malignant growth in relation to embryonic proliferation are the tumours which arise at the earliest period of life, such as nephroblastoma and sympathicoblastoma. With the exception of the fact that they occur at a period of very active normal proliferation, we know nothing as to their origin.

Some other points may be referred to in this preliminary review; one of these is the *distribution of malignancy* in the human body. Recent investigation has not only revealed more and more the wonderful variations in the structures of tumours but also the multiplicity of cells from which they may arise. One is justified in saying that malignancy may appear in any cell of the body, with one proviso, however, that the cell has the power of normal proliferation. Tumours malignant, as well as simple, arise not only from the tissues most active in repair but also, though less frequently, from the specialised cells—e.g., those of the liver, adrenals, and endocrine glands. An adult nerve-cell, on the contrary, has lost the property of proliferation and no tumour arises from it; but a growth may originate in its progenitor, the neuroblast, and often possesses highly malignant properties. The terms "carcinoma" and "sarcoma" are thus a poor reflection of the varieties of tumours. The origin of malignant neoplasms from highly specialised cells is an important section of the general subject, but so far it has been scarcely touched by experimental methods.

Another matter in relation to the general question is *age-incidence*. Malignancy becomes more frequent as age increases owing to the higher incidence of carcinomata associated chiefly with increasing opportunity for damage, irritation, and other disturbances of the tissues. But malignant growths are met with in the early years of infancy, and there is clear evidence that they may originate during intrauterine life. Interesting facts with regard to this subject have been gathered in recent papers by Blacklock (1934). Sarcomata of bone too are markedly related to the growth period. The outstanding fact, however, is that from whatever cells, in whatever way, and at whatever age malignant tumours arise, they are essentially similar in their general behaviour and in their conditions of growth. One naturally holds as a working hypothesis that there must be some ultimate disturbance of cell life underlying all the different conditions.

Ætiological Factors

When we consider the cause of malignancy, it must be recognised that the subject is of great complexity. In the first place there are the particular circumstances in time which give rise to malignancy—the primary or initial causes. There are also additional circumstances such as the susceptibility of the tissues, especially that which is hereditary; these are equally essential to the occurrence of malignancy. And finally there is the factor of the vital behaviour of the cells, whether this is a continued reaction to some agency or results from some obscure form of nuclear damage. The last question concerns the real nature of malignant proliferation. The matter may be put in the following way. Various irritant and abnormal conditions give rise to malignancy; there are numerous primary causes. But what is the causation of the malignant proliferation, say in a secondary growth, when the cells are beyond the influence of the agency which originally led to its development? Neoplastic proliferation corresponds up to a point with reactive proliferation but it seems to possess in addition a feature all its own.

Looking back on the results of research during recent times, say the last 25 years, one cannot but be impressed by the advance in knowledge of the different ways in which tumours may be initiated. Chronic irritation was the first factor to be recognised, and the cumulative evidence of numberless clinical observations became practically conclusive as to its importance. Then followed the recognition, still from the clinical side, that a number of so-called irritants, strikingly different in their nature, were specially liable to cause the malignant change. The matter was then clinched by experimental work which started with the researches by Fibiger on gongylonema cancer and those of Yamagiwa and Ichikawa on the production of epithelial new growths by tar. Since that time the number of carcinogenic agents has been steadily added to and now they are many in number and variety. I should like to say here that the contributions of workers in this country have been of a distinguished order. Real progress was made when Kennaway (1925, 1930) first established the relation of chemical structure to the carcinogenic property and showed how slight variations in the molecule might be attended by absence or presence of the property. Kennaway's observations and those of Cook and his co-workers (1932) brought out clearly that there is no relationship between irritating effect in the ordinary sense and the faculty to lead to malignancy, and hence raised the possibility of there being some common feature in chemical structure on which the carcinogenic property depends. From these and other observations it would appear, however, that the carcinogenic agents have a special property of stimulating growth or cellular proliferation, whilst other closely allied chemical substances have not this property. "Growth stimulants" rather than "irritants" would appear thus to be the preferable term. The next advance was made by Cook and Dodds (1933) who showed that dibenzanthracene, one of the most active carcinogenic agents, had an œstrogenic effect on mice like that of œstrone or folliculin. In this way a link was made as regards biological effect between a carcinogenic substance and a female sex hormone. Another step of great importance was the demonstration by Lacassagne (1932) that the injection of œstrone is effective in producing adenocarcinoma in the mammæ of male mice. These observations will be further referred to.

If I were to attempt to give a summary of the results which have been reached I might put it as follows: (1) By both experimental and observational methods it is shown that malignant growths may be produced by the prolonged action of irritants and cell stimulants. Such growths chiefly affect tissues active in repair. (2) There are malignant growths of the more specialised epithelial tissues and of some connective tissues which have not yet been produced experimentally, but pathological observations in the human subject indicate that they may arise on the same principles. (3) There are malignant growths which can be placed in neither of these two classes. We know nothing as to the conditions incidental to their occurrence and can hardly even speculate as to their causation. Such are the malignant growths arising from embryonic cells, sometimes multipotent; those of the leucocyte-forming tissue; also a great variety of tumours in connexion with the central nervous system, endocrine glands, &c. The methods of experimental embryology may throw light on some of these. The origin of malignancy in relation to normal proliferative processes, however, is a subject on which one can say nothing definite. For example, while the age-incidence of bone sarcoma indicates its relation to processes of normal growth, it is an instructive fact that bone sarcoma may also arise at a later period of life in relation to abnormal proliferative processes—e.g., those in connexion with generalised osteitis and Paget's disease of bone.

In view of the large number and great variety of chemical and physical agencies which have been shown by clinical and experimental methods to lead to malignancy, one is caused to inquire whether there is any one general principle concerned in the initiation of malignant growth. The nearest approach to a general statement which I think can be made is that the acquisition of malignancy is related to *previous non-neoplastic proliferation*. Sometimes the proliferation may not be continuous, and it is known that malignancy may appear after a person has been removed for some time from the carcinogenic influence; but the fact that the time intervening between its start and the onset of malignancy is comparatively long as a rule cannot be without significance. The occurrence of a long latent or silent period between the initial stimulus and the malignant growth is the rule. But there are exceptions; noteworthy examples are the malignant growths appearing shortly after birth, also chorion-epithelioma at a later period of life. It is interesting, however, that such tumours are related to growth of a very active kind.

I shall not discuss here proliferation following a single trauma in relation to the origin of malignant growths; it is a wide and controversial subject and has recently been treated comprehensively by Ewing (1935), with whom I agree in all essential particulars. On considering the conditions which lead to repeated or continuous cellular proliferation in pathological states we see that they are chiefly of three kinds: (*a*) chronic irritation, (*b*) compensatory hyperplasia, and (*c*) the action of hormones. Something may now be said in exemplification of malignancy occurring in these three conditions.

(*a*) The term "chronic irritation" must be used in the widest sense. There are cases of carcinoma following long-continued reactive proliferation where nothing is known of the nature of the irritant. Carcinoma of the cervix uteri may be mentioned in illustration. An interesting example of a malignant growth produced by a definite *chemical substance* is that recently discovered by my colleague, Prof. Browning, and his co-workers (1936). The substance in question is a water-soluble styryl compound, chemically unrelated to the carcinogenic substances of Kennaway and others, and an interesting point is that sarcoma has followed a single injection in a large proportion of cases. When injected subcutaneously the dye becomes precipitated in the tissue fluid and minute coloured particles are formed but there is almost no immediate irritant effect. Some months later a perceptible induration is present at the site, and this is due to tissue formation constituted mainly by large masses of phagocytes containing the coloured particles. Later still, rapid growth occurs owing to development of sarcoma which is of the spindle-cell or pleomorphic type. The growth has been transplanted to other mice, in one case ten successful passages have been made. The special features here are the relative lack of initial irritant effect and the very slow growth of the reacting cells up till the time of the appearance of malignancy.

(*b*) In the second place, reference will be made to malignancy as a sequel to *compensatory hyperplasia*. The importance of this is that *specialised* cells proliferate. There are fewer definite examples of this

but a noteworthy one is met with in the liver. Probably no other organ responds so readily to loss of its substance by compensatory growth; the loss of a third or even half of its bulk experimentally produced, is soon followed by restoration practically to the original weight. The same compensatory process occurs when there is destruction of the liver cells by disease, as in cirrhosis, and then not rarely the compensatory process passes into malignant neoplasia. I studied this and was able to follow the stages (1908). The cells in a hypertrophic focus on acquiring malignancy show alterations both in cytoplasm and nuclear structure. A liver trabecula, which may be regarded as a tubular gland with a bile capillary as its lumen, becomes changed into an elongated mass of cells without lumen, while the cells become altered in appearance. A break through then occurs and a liver-cell carcinoma results. This may happen in multiple foci. To what extent a similar process may occur in growths from other specialised cells is uncertain, but the same principle may hold in the case of endocrine glands. In the thyroid, for example, carcinoma is definitely related to goitre, and this in turn depends upon a succession of processes of hyperplasia and involution.

(*c*) I shall now say something with regard to malignancy as a sequel to proliferation produced by hormones. A new field of inquiry has been opened up by the work recently done on this subject. The malignant growths thus produced have been in the mamma and, as the results enable us to interpret the changes found in human disease, I shall first describe my observations bearing on the general question.

Malignancy in the Mamma

The subject may be arranged under three headings: (*a*) the development of malignancy in the mamma; (*b*) the struggle between malignant cells and the normal tissues; (*c*) the parasite-like behaviour of the cancer cells.

DEVELOPMENT

The development of malignancy has been studied in breasts the seat of manifest cystic disease, in those with various conditions of local hyperplasia and fibrosis with little or no cyst formation, and also in those in which actual carcinoma is present. In the last mentioned the non-malignant changes are of special importance in relation to the development of carcinoma. As a result of such study one becomes convinced that there are a whole series of structural changes presenting infinite variety as regards detail, which affect the mammary epithelium and lead up to malignancy. To speak in the most general terms, these are (1) increased and altered secretion accompanied by changes in type of the epithelium, and by desquamation of cells, and (2) hyperplastic proliferation of the epithelium. These are, of course, associated with fibrosis in varying degree. Whilst disordered secretion, leading to distension of ducts and acini, appears often to be the initial change, the degree in which either of the two kinds of epithelial changes predominates varies in different cases. Sometimes cyst formation is the outstanding feature, resulting in the so-called cystic degeneration or Schimmelbusch's disease. More frequently hyperplastic changes predominate and these are of special importance in relation to malignancy. Cheatle (1926, 1931) has already given a full account of the changes and I agree with him on all essential points.

The hyperplasia of epithelium is attended for a long time by a coördinated increase of connective tissue—a condition still removed from malignancy. Thus there arise papillomatous growths in the ducts and these are often present at an early stage in association with cystic dilatation. The papillomata may be small and numerous or they may reach a considerable size. The well-known duct papilloma, for example, may be associated with relatively large papillomata in the substance of the breast. The next stage is a relative overgrowth of epithelium in comparison with stroma; epithelial outgrowths are now produced which contain only a small amount of connective tissue. This condition passes on gradually to a stage where there is proliferation of epithelium alone and large cellular masses without any stroma are found within the ducts. For a time the epithelial cells, though enlarged, show little alteration in their characters and mitoses are few. Further, the cells retain their polarity to a certain extent; some are columnar and form rings or pseudo-acini in the cell masses (Fig. 1). Occasionally the hyperplasia affects only one side of a duct (Fig. 2). Finally the anaplasia becomes distinct; the cells and their nuclei vary in size, the latter becoming of the vesicular type with distinct nucleoli. The amount and arrangement of chromatin vary and ultimately one finds within the ducts cellular masses which have all the characters of an encephaloid carcinoma (Fig. 3). The term *intraduct carcinoma* may be then applied as we are justified in regarding the cells as malignant although they have not yet passed into the tissue spaces. Such changes may be met with at different stages in the same case and may be accompanied or not by carcinoma.

The statement is not infrequent that intraduct carcinoma is rare. Its occurrence as a widespread condition, giving rise to the so-called comedo masses within the ducts, is relatively uncommon. But local intraduct carcinoma is in my experience quite common, being found in many cases of carcinoma of the breast as well as in cases free from carcinoma. In association with the changes in the ducts a few acini are commonly affected similarly but occasionally there is a growth of malignant cells within the acini over a considerable area. The epithelium of the acini may be entirely replaced by cells of malignant type whilst the structural outlines of the acini are completely retained, a condition of intra-acinous carcinoma. Such a condition may be extensive, whilst alongside there are lobules of normal appearance (Fig. 4). I believe that intraduct carcinoma with or without intra-acinous carcinoma represents a condition where the cells have acquired the characters of malignancy yet are still within normal bounds—a sort of pure culture of malignant cells but still within test-tubes, as one might say. It is usually a process of very slow development; it is often relatively static and may exist for years. Ultimately the natural consequence is the break through the normal confines with an ordinary infiltrating carcinoma as the result. This probably happens more frequently from the ducts as they are so much oftener affected. On the other hand, when acini are affected break through will take place more readily owing to the slighter resistance afforded by their walls.

One may ask—why do the cells not break through at once? Reactive changes in the walls of the ducts play a part, but sometimes they are absent; and the basement membrane of an acinus would appear to be but a slight barrier. The supply of nourishment will also be concerned and it is evident that the malignant cells will be in a much more favourable condition in this respect when once they are in the tissue spaces. It is, however, clear that there may be a balance between tissue restraint and malignancy

ILLUSTRATING CHANGES IN THE MAMMA BEFORE OCCURRENCE OF CANCEROUS INFILTRATION OF THE TISSUES

FIG. 1.—Duct showing marked hyperplasia of epithelium without stroma; cells still show polarity and tendency to form circles. (× 100.)

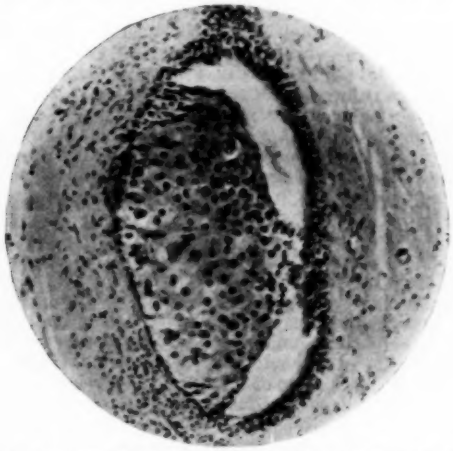

FIG. 2.—Localised precancerous epithelial hyperplasia in small duct; several similar foci were present. (× 150.)

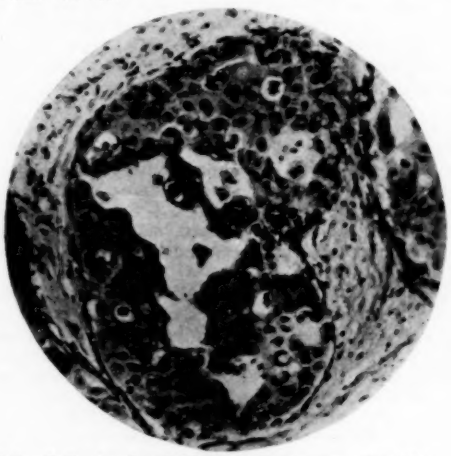

FIG. 3.—Fully developed intraduct carcinoma. (× 150.)

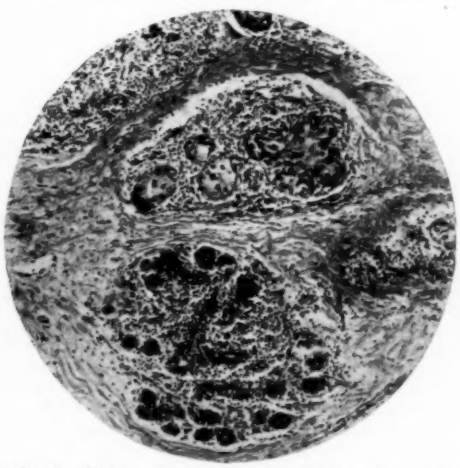

FIG. 4.—Above, group of acini showing intra-acinous carcinoma; below, unaffected acini. (× 75.)

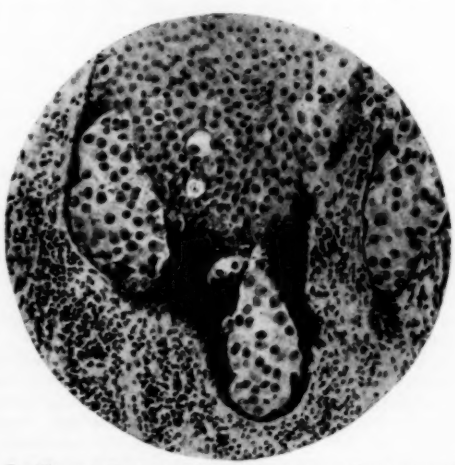

FIG. 5.—Masses of cancer cells within interpapillary processes of epidermis of nipple—"Paget" lesion; also separate cancer cells. Secondary to intraduct carcinoma. (× 150.)

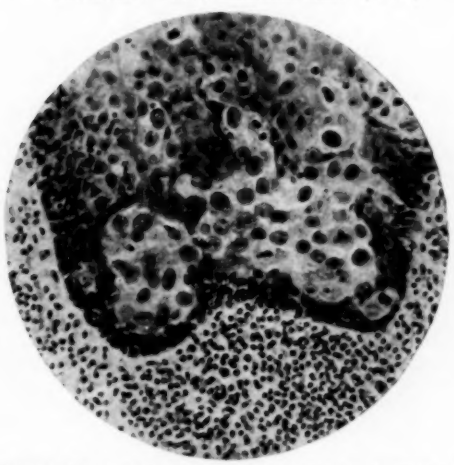

FIG. 6.—Mass of cancer cells in deep part of epidermis, showing several mitoses (from same case as Fig. 5) (× 200.)

for a long period. The same holds when the malignant cells reach the epidermis and produce Paget's disease.

It may seem strange, almost incredible, that intraduct carcinoma may exist for some years before infiltration occurs, but it is not so strange if one bears in mind how many years may elapse before there is recurrence after operation, that is, before cells actually infiltrating have been again able to produce a manifest growth. I shall add only one other point. From a picture of malignant cells within the mammary ducts one can readily understand how trauma may set up actual invasion.

STRUGGLE BETWEEN MALIGNANT CELLS AND NORMAL TISSUES

This struggle has often been observed and is of two main types. In the first place, the presence of malignant cells within ducts may give rise to reaction of the connective tissue inside the elastica. This tissue often undergoes a laminated thickening leading to diminution of the lumen, and as it progresses the cancer cells are gradually strangulated, as it were, and ultimately disappear. The condition corresponds with a chronic endarteritis proceeding to complete obliteration. This process has been described and figured also by Cappell (1931). In the second place, there may occur a marked cellular reaction around the affected ducts and also around affected acini, the cells being chiefly plasma cells and lymphocytes. At places these may penetrate the walls of the ducts and as this occurs the elastic tissue disappears. The contained cancer cells are then invaded and again they may undergo atrophy and disappear; fibrosis of the newly formed connective tissue follows. The result of either process is that obliterated ducts come to be represented by a relatively acellular core of hyaline tissue surrounded by markedly hyperplastic elastic tissue. Ducts in this condition are of common occurrence both when intraduct carcinoma alone is present and also when infiltrating carcinoma has supervened. I cannot say that ducts in this state are always the result of effete intraduct carcinoma but there is no doubt that this is often the mode of development. The same sort of cellular infiltration as that described is seen also round intra-acinous carcinoma, and it would almost appear as if the cells in the malignant state had a chemotactic influence on the lymphocytes and plasma cells. Malignant acini may be invaded by them and all stages up to complete disappearance of malignant cells may be followed. Such processes of healing are of course effective only here and there and the disease as a whole is progressive. Nevertheless they illustrate well "the conflict between malignant cells and the normal tissues."

THE CANCER CELL AS "PARASITE"

The parasite-like behaviour of the cancer cell is only a descriptive term without reference to the ultimate nature of malignancy. A striking example is the growth of cancer cells within non-neoplastic epithelium which is found in those rare cases where the cells of an underlying carcinoma invade the epidermis and then spread within the latter just like parasites, occurring in clumps and also as isolated cells. I show you coloured photomicrographs † from the case published by Shaw Dunn (1930). The tumour is a mucoid (colloid) carcinoma and has been stained by mucicarmine. You will see at a glance the cancer cells stained red within the epidermis, especially in the deeper layers; a great many cells are quite isolated. Such a mode of spread is, however, commonest in connexion with intraduct carcinoma, and in my opinion it is the basis of Paget's disease of the nipple.

The distribution of the malignant change within the ducts depends in part on multiplicity of foci and partly on the manner of spread, and the latter includes the intra-epithelial route. To put the matter briefly, once the cells have assumed malignant properties they may infiltrate the lining epithelium and grow within it. The malignant cells again behave like parasites and the epithelium plays a passive rôle. The epithelial cells invaded are in fact compressed by the malignant cells though they may be recognisable for some time by their flattened and atrophied nuclei. One may see large oval malignant cells with characteristic nuclei growing in an isolated manner here and there, or they may form a continuous sheet of cells covered by a persisting layer of the original epithelium. I have traced this mode of intra-epithelial growth at all stages and in all parts of the mammary tissue. I have seen it within acini, in the small and large ducts, in the ampullæ and large ducts of the nipple. It is more frequent in the last-mentioned situation, possibly because the epithelium there has a purely lining function to the pathways and presents more resistance to the spread. I have seen isolated malignant cells confined to the epithelium at the orifices of the ducts where the cells first arrive at the epidermis. Spread then occurs in the latter, producing the Paget lesion, and the peculiar appearances of the invading cells are simply due to their growing in a comparatively resistant epithelium. Sometimes, however, the growth is of an active type (Figs. 5 and 6). I need not go further into details as I have described them elsewhere (1927, 1935); the point that I wish to emphasise is that the parasite-like behaviour of the malignant cell is brought out in a striking manner in these conditions and situations.

PRECANCEROUS CHANGES AND THE ENDOCRINE FACTOR

A considerable diversity of opinion still prevails as to the relation between cystic disease and carcinoma. One can approach the question from two points of view. From the clinical side one can follow up cases of cystic disease and find the incidence of carcinoma in these. The results obtained by this method are somewhat conflicting. On the other hand, one can study histologically breasts in which carcinoma has already developed and search for evidence of precancerous changes. My experience is that with the latter procedure it is the rule to find epithelial hyperplasia on the basis of which malignancy has developed. The epithelial growth is often associated with cysts but these may be of microscopic character and more frequently still would not be recognisable as such during life. Malignancy may develop in connexion with large cysts, but epithelial hyperplasia is the all-important factor, and although the two types of lesion, cysts and hyperplasia, may coexist sometimes in striking fashion, I think that they are often in inverse proportion to one another.

To interpret the above changes as the usual precursor of malignancy agrees with what we know regarding malignant disease elsewhere and especially with the results of experimental work on carcinogenesis. In the complete absence of evidence that the changes are of inflammatory nature produced by some outside agency, it was natural to regard them as in some way the result of endocrine disturbance, though it seemed more difficult to apply this

† The lecture was illustrated by lantern demonstration of photomicrographs in colour.

explanation to the numerous examples of localised hyperplastic change. Such a view is in agreement with what had been demonstrated with regard to endometrial abnormalities. I shall refer briefly to what has been established.

The effect of folliculin or œstrone on the resting mamma was first, I believe, described by Goormaghtigh and Amerlinck (1930), who demonstrated the important effect of the hormone in producing growth. Lacassagne (1932) was, however, the first to show that carcinoma may be produced by repeated administration; this has been confirmed by Burrows (1935), Bonser (1936), and Cramer and Horning (1936) in this country. Lacassagne showed that in the case of male mice of a susceptible strain the incidence of carcinoma was very high, but malignancy developed also in a proportion, though much smaller, of unselected mice. Briefly one may say that œstrone causes in the male mouse a growth of the relatively atrophic epithelium of the ducts of the mamma, this growth being often attended by dilatation and accumulation of a colloid-like secretion. The epithelium also may show hyperplastic changes and occasionally there may be a growth of small intraduct papillomata. There may be accompanying growth of acini from the extremities of the ducts and a considerable portion of glandular tissue may thus develop, this resembling what occurs in the female mamma at the time of full sexual development. These are the essential changes, and from an examination of sections kindly lent me by Dr. Lacassagne and Mr. Burrows I consider that they belong to the same category as those in the human disease. Accordingly, the male breast is in a sense changed into a female breast, and thereafter the tendency to development of carcinoma makes itself evident. Inherited susceptibility plays a very important part but the carcinogenic action is manifest, though to a less degree, in animals of ordinary strains. Here we have an example of the remarkable effect of a hormone affecting a tissue specifically related to its action. The proliferative changes followed by malignancy in a sense correspond with those produced in other tissues by carcinogenic agents, but in the present case it is to be noted that the agent is not applied directly to the tissue in question but is carried to it by the blood stream. There is thus, as I have said, a specific relationship between the œstrone or other compound and the mammary tissue.

One must however be cautious in interpreting the significance of these results. The two important points are that proliferation brought about by a growth-producing stimulus goes on to malignancy and also that the action of the agent is of a peculiarly selective kind. It does not follow from such experiments that the changes in the human breast are the result of œstrone in excess. It is known, for example, that lutein also is concerned in the mammary changes in connexion with menstruation and pregnancy, and our knowledge is at too early a stage to allow any opinion as regards the mode of production of hyperplastic cystic disease. Nevertheless the facts give strong support to the view that cystic hyperplasia is the result of disordered endocrine balance. Advancing knowledge goes to show that this balance is of a very delicate kind. It is interesting to note that Cramer and Horning have found that the repeated administration of œstrone may produce an adenomatous condition of the pituitary—another example of the interdependence of the endocrine system.

It is thus seen that malignancy may arise in different ways—it has in a sense many different initial causes—and that previous reactive or non-neoplastic proliferation is a common and important factor. An analogy is sometimes drawn between the inflammatory process and the cancerous or malignant process. Each undoubtedly results from many diverse causes and each is incapable of ultimate explanation. But in inflammation there is a combination of cell proliferation, tissue formation, phagocytosis, &c.; the changes are directed towards the defence or repair of the tissues and are representatives of processes normally in operation. Inflammation, in fact, may be regarded in chief part as evolved for the benefit of the organism, and though, like malignancy, it often cannot be controlled, it is regulated by the presence of the irritants or micro-organisms, and on their removal or destruction it comes to an end. In malignancy, although there may be no phenomenon new in kind, the intensity and autonomous character of the proliferation, resulting usually in the death of the organism, is in certain respects a unique phenomenon. Why is the growth not controlled by the normal agencies? I shall now discuss this question.

Essential Nature of Malignancy

With regard to the essential nature or cause of malignancy there have been many theories. Any theory must of course be applicable to all the known facts and must also stand every experimental test. With advance in knowledge views formerly held have had to be put aside and there are now two main theories. The one is that malignancy is the result of a change in the mechanism of the cell; the other is that it is produced by the presence of a virus. The first of these has been held by many, and within recent years has been brought into prominence by Boveri (1933), who described the change as a definite "abnormal chromosome-complex," or as Murray puts it, "an invisible, partial damage to individual chromosomes." It has been modified by Lockhart-Mummery (1934) in the form of gene mutation of somatic cells. I would prefer, however, to avoid the use of terms which may have a connotation not strictly applicable to malignant growths. The essence of all such theories is that the cell mechanism has undergone a change, evidently in the nucleus, which is apparently permanent and transmitted to the cell descendants. In this form the theory is little more than a summary of the facts already discussed. The change in the cells, which be it noted is in at least most instances produced by environmental conditions, appears to be twofold. In the first place there is the escape from the normal growth-controlling agencies of the body. In the second place there are the altered characters of the cells which give the tumour its special structural characters. Both of these alterations are transmitted in series and the first is manifestly of a very fundamental kind.

The parasitic theory has passed through many phases. The coming of bacteriology and the establishment of the relationship of bacteria and other micro-organisms to granulomata naturally suggested that malignant tumours were brought about in a similar way; and the idea of an extraneous agent as the cause was to many more satisfying than the hypothesis of altered cellular mechanism. Various organisms have been put forward—protozoa, bacteria, yeast, &c.—but it is now generally recognised that if a parasite is concerned it can only be an invisible micro-organism such as a virus. No definite pronouncement can be made on the subject but some established facts with regard to the virus theory may be considered.

THE VIRUS THEORY

The discovery of Peyton Rous in 1911 that in fowls a sarcoma can be transferred by a cell-free filtrate is a fundamental one in biology and starts a new era in connexion with neoplasia. It was thus shown that malignancy can be transferred apart from the medium of living cells, the latter method having been up till that time the only one by which it could be effected. As is well known to you, the sarcoma occurred naturally in a fowl, and since that time a considerable number of filterable tumours in birds have been discovered—sarcoma, osteosarcoma, endothelioma, &c. Nothing is known as to the origin or initial causation of the natural growths and there is no evidence that they are passed from bird to bird like an infection; they occur sporadically. They have all the characters of malignant neoplasms, and the only peculiar feature is that they can be transferred by the agency mentioned. The filtrates of such growths are specific in the sense that they are active only in birds of the same species or in closely allied species; in this respect there is a correspondence with what obtains in the case of transplantation by living cells. The filterable agent has another characteristic feature—namely, that it reproduces in specific form in the new growth the characters of the original growth.

It is important to realise that the filterable agents in these tumours cannot be placed in the same class as the carcinogenic agents. The former produce malignant proliferation almost at once and, what is of greater significance, they are reproduced or increased in amount as the tumour grows. Carcinogenic agents have done their work when they have started malignancy; they are not present, for example, in the secondary growths. The filterable agents, on the other hand, both start and maintain the malignant proliferation and are present in the tumour tissue wherever it is. Two questions thus arise: first, what is the nature of the filterable agent, and second, to what extent can the results established with regard to these growths be applied to malignant tumours in general?

Gye (1925), from his observations, put forward the view that the filterable agent is of dual nature. There is a specific factor formed by the tumour cells—specific for the type of growth and produced in them as malignancy develops. There is also a virus which is common to malignant neoplasia in general but which for its action requires the coöperation of the specific factor. This view theoretically is in accordance with the facts stated above, but all attempts to prove definitely the dual nature of the filterable agent have so far been unsuccessful. If this is to be the ultimate result, is it possible to explain the facts on the assumption that there is a single agent? Whether is the virus or the specific factor to be retained? According to Gye's theory the specific factor produces the structural characters of the growth, but it has a further effect—it induces the cell to produce more of itself. In other words, there is an increase of the specific factor as the tumour grows, thus there is a resemblance to multiplication. There remains to be considered only the effect supposed to be due to the virus—viz., the cell proliferation induced. In view of what is known with regard to hormones and other substances, may not the specific factor, seeing that it is reproduced, be the cause also of the uncontrolled growth?

If the filterable agent is a virus the question arises—is there one or are there many? On the supposition that there is a single virus one great difficulty presents itself owing to the fact that it produces in the new tumour the features of the tumour from which it comes. That a virus should be modified by the tissue in which it has gained a footing and grown is in accordance with what we know, but that it should, as it were, carry with it the characters of its environment in the original growth to a normal tissue is a phenomenon to which so far as I know there is no parallel. If, on the other hand, there is a multiplicity of viruses or a virus for each tumour, we are left with insuperable theoretical difficulties, which were met by Gye's view as to the dual nature. The filterable agent corresponds in many of its properties with a virus or living organism, and the majority of workers on the subject accept the virus theory. Others, however, consider that its virus nature has not been established. Murphy (1926), for example, believes that it is a cell product which he considers a transmissible mutagen; this is at least a descriptive name for Gye's specific factor. These seem to me the essential facts bearing on the subject, but I may refer to one or two other points.

What is required in this field of inquiry is some method of definitely recognising a virus. Suggestive experiments have recently been published by Ledingham and Gye (1935) with regard to this. In the case of the Rous sarcoma they have centrifuged at high speed the infective fluid and have demonstrated in the sediment elementary bodies similar to those found in vaccinia and other virus diseases. Moreover the infectivity of any portion of the fluid is in proportion to the number of such bodies. These results at once raise the question whether such bodies can be seen in other kinds of malignant growths and especially those which are produced experimentally by carcinogenic agents. Time alone will supply the answer but the result, whatever it may be, has an important bearing on the problem as to whether the fowl tumours occurring naturally and those produced artificially are alike in this respect. It may be noted too as another point of interest that intranuclear inclusion bodies resembling those seen in certain virus infections have been observed in some tumours by Dorothy Russell (1932) and others.

An all-important question is whether there is a filterable agent in an artificially produced fowl tumour, as contrasted with a naturally occurring tumour such as the Rous sarcoma. As an example, dibenzanthracene in lard or some other vehicle is injected into the breast muscle of a fowl; in a short time the dibenzanthracene is no longer demonstrable at the site (Chalmers, 1934); some months later a sarcoma develops—a remarkable series of events. Can a tumour be set up in a fresh fowl by injection of a filtrate of an emulsion of the tumour thus produced? Peacock (1935) has carried out a large number of experiments on this subject with great care and persistence, and the results have been uniformly negative; he has been able to find no evidence of a filterable agent. McIntosh (1933), on the other hand, has obtained three positive results. This is another problem to which a definite answer cannot be given; we must await further evidence. If it is found possible to transmit such artificially produced tumours by the method mentioned, this might be due again to a product of the malignant cells or to a virus secondarily invading the proliferating cells and rendering them malignant. In the latter case the question arises as to the origin of the virus and the method by which it has reached the site of inoculation, and this will be referred to below.

VIRUSES AND MAMMALIAN TUMOURS

The general facts with regard to tumours produced by a cell-free filtrate correspond in a striking way

with those observed when transplantation of living cells is the agency. The filterable agent has been found only in some connective tissue and endothelial tumours of birds; in other instances such growths have not been filterable. So far as I know, there have been no undoubted examples of transference of a mammalian tumour by this method. This restriction in occurrence does not weigh greatly with me; it does not imply that the filterable tumours are in nature different from other growths. It is well known that a filterable tumour may lose its filterability and again regain it. The negative results in the case of epithelial growths too are not surprising since, owing to the difficulty of bringing the neoplastic agency sufficiently long in contact with the homologous epithelium, the test is an exacting one.

The domain of viruses as pathogenic agents is gradually being extended by investigation, and some definite tumours have been shown to be caused by them. A recent example is the work by Peyton Rous and Beard (1934) on Shope's infective papilloma of the cotton-tail rabbit in America. This growth is undoubtedly caused by a virus; under natural conditions it spreads as an epidemic and the lesion can be artificially propagated by scarification. Now if a portion of such a papilloma is transferred into the internal tissues or organs of rabbits, the appearance of an infiltrating epithelioma is produced. More recently they have shown that papillomas induced in domestic rabbits by the virus progress to malignancy in a considerable proportion of cases. These are interesting results; how are they to be interpreted? It can be demonstrated that the virus is present in the epithelioma since a papilloma results when the skin of a normal rabbit is inoculated from such an epithelioma. The problem here comes to be quite a definite one—does the malignancy of the epithelioma, that is the uncontrolled proliferation of its cells, depend upon the presence of the virus or has the virus produced malignancy as other carcinogenic agencies may do, the virus then merely persisting in the malignant growth? In other words, if the virus could in some way be removed from the epithelioma, would malignancy persist or would it come to an end? Till this is answered it is not possible to assess the general bearing of the observations.

I have given briefly the chief facts relating to the subject and it is not possible to give definite answers to the question put above with regard to the nature of the filterable agents in fowl tumours and their relation to other growths. Certain fundamental facts have been established and one would like to be able to bring them into harmony with our knowledge of malignant tumours in general and give a comprehensive view, even if it were merely theoretical. At present this does not seem possible. But if we consider as a whole the results with regard to carcinogenesis and the filterable growths, there is no valid evidence that malignancy in general is produced by a virus or viruses entering the body *from outside*. The experimental facts appear to exclude this possibility. This is a matter of great practical as well as theoretical importance. Malignant growths can be set up by carcinogenic agents so regularly, not only when they are applied externally but when they are introduced into the tissues, that the access of a virus from without on each occasion seems impossible. The high percentage of growths produced in cancer-susceptible strains of mice by means of œstrone is a specially significant fact in this connexion. Even if it were supposed that a virus were a practically ubiquitous commensal on the skin and mucous surfaces, this would not explain the regularity with which growths may be produced in the deeper tissues. It may be that some human malignant tumours are due to viruses entering the body from outside, but this does not affect the general question.

The matter has been investigated too from the experimental side. Rous and Botsford (1932) reared mice from birth in a sheltered condition—that is, they were protected against the entrance of any infective agent from without, though the growth of commensal bacteria such as coliform organisms or cocci was not prevented. It was found that in such mice repeated applications of tar led to the development of epithelioma just as readily as in normal mice. We thus seem to be driven to the conclusion that if a virus is necessary for malignancy it must be present within the normal tissues in the interior of the body and act only when proliferation has been previously set up by carcinogenic agents or in some other way. Various supporters of the virus theory have been forced to this view; it has recently been expounded by Andrewes (1934) and the facts bearing on it have been marshalled by him. It is a hypothesis on which nothing definite can be said. No one can prove or disprove the presence of a virus in normal tissues ready to produce malignancy when occasion offers. It must be noted however, as has been already mentioned, that in addition to uncontrolled proliferation there are alterations in the characters of cells which are transmitted to their descendants. The experimental work on cancer in the mouse shows clearly that the cells of a malignant growth breed true both as regards their characters and rate of growth. As Murray (1933) puts it, the growths show "a continuous graduated series in those arising from any one tissue both in histological structure and in rate and habit of growth. In spite of this great range any one variety is relatively permanent." Can this impress resulting in special features be made by a single virus? No one doubts that such an agent as œstrone of itself produces the hyperplastic changes in the mamma, varying greatly in different cases, and a virus, if one there be, can come into play and produce uncontrolled proliferation only when these essential changes have occurred. It seems to me that transmission of permanently altered cell characters must also be a necessary factor. The same applies to growths in the human subject. The numerous and practically endless variety of histological types must be due to forms of proliferation and hyperplasia brought about by the various agencies referred to, aided of course by congenital abnormalities and inherited susceptibility.

IGNORANCE AND KNOWLEDGE

Each of the two theories has its strong supporters but a decision is not to be arrived at by the votes even of so-called authorities. On either view there seems to be a failure on the part of nature. In the one case normal proliferative processes evolved for defence and repair—one may say, "for the good of the organism"—pass into malignancy. In the other case the animal body has somehow come to harbour a virus or viruses which, given certain opportunities, lead to its destruction. It may seem that for practical purposes it is immaterial which of these two hypotheses is correct; nevertheless, the demand for intellectual satisfaction is and always will be insistent. The problem seems to be in a realm which we have not yet the means of entering, and some think it is incapable of solution. But no one conversant with the advances in recent times can doubt that at least fresh light will be thrown on the subject.

In what I have said a sharp distinction has been

made between the conditions which induce malignancy and the real nature of malignancy or, as one may say, the essential cause of the uncontrolled proliferation. If we are held up for the present by our ignorance of the latter the advances in our knowledge of the former have brought results which have an important practical bearing. I remember some thirty years ago hearing an authority on tumour growths discuss the question whether neoplasia could arise in tissues previously normal. We have now moved far from such a standpoint. The advances in knowledge during that period have been numerous and substantial and in the main due to the experimental method. There have been three main phases of experimental investigation—first, the transference of naturally occurring malignant growths by transplantation of their cells into normal animals, and the conditions and limitations of such transference; second, the methods of starting malignancy de novo; and third, the transference of tumours by means of a filterable agent. In all three departments much has been accomplished.

The fact that the problem as to the essential nature of malignancy has not been solved has unjustifiably obscured what has actually been achieved. That malignancy may supervene on cellular proliferation brought about in various ways, by irritants, cell stimuli and hormones, and as a result of compensatory hyperplasia; that in most cases a long period elapses between the onset of proliferation and malignancy; that in the case of chemical substances the tendency to institute malignancy is in certain instances related to molecular structure; that inherited susceptibility plays an important part especially in certain organs; that the development of malignancy depends in some cases upon congenital abnormalities, and that these factors may be combined in different ways—these are facts which have been completely established.

Knowledge of causes brings with it the possible means of prevention and has already been effective. Recognition of the necessity for an intimate study of growths, simple and malignant, in every organ and region of the body is clearly shown by the publications of the present time. And in investigating what I may call the natural history of neoplasia close coöperation between clinical observers and pathologists is essential for the attainment of the best results.

I see much that is hopeful. In the various departments of inquiry to which I have made reference fresh stimulus has been supplied by recent advances. It is natural, in fact it is right, that workers in any one field should push the implication of their results to the full, but all results must be coördinated and tested in relation to the fundamental questions. The picture I have endeavoured to present has come chiefly from researches in the last twenty-five years. I have little doubt that in another similar period it will be greatly changed and that what I have brought before you in this address will be only a record of what has been.

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VITAMINS IN HUMAN NUTRITION

THE EXCRETION OF VITAMIN B_1 IN HUMAN URINE AND ITS DEPENDENCE ON THE DIETARY INTAKE

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IN the past the assessment of malnutrition, or of "suboptimum-nutrition," has been based largely on measurements of physique; various alternative formulæ have been proposed by which numerical expression may be given to the weight-height or weight-age relationships. The clinical appearance, and to a less extent the physical performance,[1] are two other criteria most commonly used. To-day, however, the realisation is growing that more specific tests should be available to establish the presence of any given type of dietary deficiency. Not only is it important when a child is undernourished to know which specific dietary errors are responsible, but—more important—it has to be realised that partial deprivation of an essential factor may not lead to any obvious symptoms of ill-health at all for some considerable time to come. In the latter case then a specific test for a given vitamin or other nutritive element may give the first evidence that nutrition is in fact suboptimal.

For vitamin C it has already been shown that the amount excreted in the urine [2 3] may serve as the basis for a test. Subjects suffering from avitaminosis C cease to excrete vitamin C in their urine and in contrast with normal subjects fail to give a urinary peak of response after the administration of a suitable test dose. Quantitative data for the excretion and response to test doses have now been determined for subjects given the reputed "minimal" or "optimal" doses of vitamin C.[3] With the object of

(*References continued from previous column*)

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elaborating similar methods for vitamin B_1 the experiments to be recorded below were undertaken.*

Past work.—Very little information of a quantitative nature is available in the past literature as to the amount of vitamin B_1 in urine. Muckenfuss [4] in 1918 concluded from feeding tests on pigeons that "the antineuritic vitamin . . . is present in fresh filtered human urine in traces apparently." Although similar experimental results were obtained by Gaglio [5] in 1919, he, on the other hand, supposed that this action upon the pigeons was due to some non-specific substances and not the vitamin itself. In view of this uncertainty van der Walle [6] reinvestigated the question in 1922 and concluded from pigeon feeding tests that "a small quantity of antineuritic vitamin is present in the [human] urine." When he fed a dog on a vitamin-free diet the urine lost its curative power. More recently, a preliminary note by Helmer [7] states that the presence of vitamin B_1 in human urine can be detected by a growth-test on rats; he fed the evaporated equivalent of one twenty-fifth part of the total daily output of urine and an appreciable growth response was seen.

Technique

It early became apparent that some method of concentrating the vitamin B_1 from the urine was necessary before it could be tested satisfactorily on the experimental animal. After a trial of various alternatives, we found that the following very easy procedure sufficed—namely, to shake the urine with "acid clay" in order to adsorb the vitamin, and then feed the activated solid direct.

TABLE I

Quantitative Control of Method. Adsorption of Added Vitamin B_1 from Urine

Amount of crystalline vitamin B_1 HCl added, in γ, to 100 c.cm. of vitamin B_1-free urine.	Amount found adsorbed, γ.	Percentage recovery.
2	1·9	95
5	3·7	74
5	3·7	74
5	5	100
10	7·5	75
10	9·3	93

Control tests (Table I.) show that with this method under suitable conditions the great bulk of the vitamin B_1 is removed by two such successive adsorptions. Specimens of 100 c.cm. of urine were first autoclaved at pH 10 for 4 hours under 2 atmospheres pressure, in order to destroy the vitamin B_1. To the autoclaved urine various known amounts of crystalline vitamin B_1 hydrochloride were then added. The reaction was adjusted to pH 5, and two successive adsorptions carried out by the addition of two lots of 1 g. of acid clay. The two specimens of activated clay were then combined and fed to rats in the manner described below.

Other adsorbents were tested under similar conditions (pH 5, 20° C.) as possible substitutes for "acid clay," but were found less effective (Table II.). Further control tests showed that the adsorption was best carried out in the region of pH 5 (Table III.).

Details of technique.—The full 24 hours' specimen of urine should be collected, preferably under a few cubic centimetres of toluene added as preservative. The total day's volume is noted, and the reaction is adjusted to about pH 5 (brom-cresol-green may be used as indicator) by the addition of a few drops of HCl as necessary. An aliquot part of the urine is taken for estimation (normally 100 to 200 c.cm., depending whether the total daily volume is low or high; or 50 c.cm. if the diet is rich in vitamin B_1, as after a test dose). One gramme of Clarit acid clay (obtained through the kindness of Messrs. Lever Brothers Ltd., Port Sunlight) is added. The mixture is shaken on an automatic shaker for 15 minutes and filtered. The filtrate is treated with a further 1 gramme as before, shaken and filtered again. The two specimens of activated clay are combined and tested direct on the rat, mixed in with a small fraction of his basal diet.

TABLE II

Comparison of Various Adsorbents

—	Amount of vitamin B_1 found adsorbed (in international units) from 100 c.cm. of urine.	
	Urine specimen 1.	Urine specimen 2.
Acid clay	2·4	3·3
Fuller's earth (E. Merck)	0·7	1·4
"Norite" charcoal	—	2·4
Vegetable charcoal ("medicinal")	0·9	—

TABLE III

Influence of pH on Adsorption of Vitamin B_1 from Urine

pH.	Amount of vitamin B_1 found adsorbed in I.U. (1 g. acid clay added to 100 c.cm. of urine).
2	1·0, 1·4, 1·4
5	1·4, 1·4, 1·4, 1·9
7	1·4
9	0·5

TABLE IV

Effect of Storage on Vitamin B_1 in Urine

—	Amount of vitamin B_1 found, I.U. per 100 c.cm.		
	Sample—		
	1	2	3
Fresh urine	0·5	2·4	1·9
After 48 hours' standing—			
No preservative	—	1·9	1·4
With chloroform	0·5	2·6	—
With toluene	0·5	2·4	—

As will be seen from Table IV. the presence of toluene is sufficient to preserve the vitamin from destruction, for several days at least. Further, the activated acid clay if dried retains its full activity even after 3 months' storage in a refrigerator (Table V.). This finding is of interest as it suggests the possibility of having assays on the patient's urine carried out at a distance whenever there are no local facilities for the animal test—e.g., in the East where beriberi is prevalent. Such work is at present in progress (see below).

Animal test.—Because of its rapidity, convenience, and accuracy the "bradycardia" method (Harris) [8-10] seems most suitable. The irregularities and "scatter" inherent in the pigeon method are obviated, and in contrast with the rat-growth method only a single dose of supplement has to be administered, and results can be obtained in the course of a few days instead of several weeks (i.e., the rats being available, ready prepared at the time of the test). Another

* The methods available for other nutritional factors will be discussed in a separate note (Harris) to be published shortly in THE LANCET.

advantage is that the same rat can be used repeatedly for separate tests. The error of the method is no more than about 15–20 per cent., which compares very favourably with most biological methods.

TABLE V

Stability to Storage of Vitamin B_1 Adsorbed on Acid Clay

—	Amount of vitamin B_1 found, I.U.		
	Specimen—		
	1	2	3
Initial value, freshly adsorbed ..	1·0	1·4	2·4
After standing—			
2 days	1·0	—	—
3 ,, ...	—	1·4	2·4
12 ,, ...	—	1·4	—
18 ,, ...	—	1·4	—
71 ,, ...	1·0	—	2·4
82 ,, ...	1·0	—	—

Young rats weighing about 50–60 grammes at time of test are used, having been placed on the standard vitamin-B_1 free diet when about 45–50 g. As soon as their heart-rate, as measured in the electrocardiograph (Clifton Instruments Ltd., Clifton, Bristol),† has fallen from the initial value of about 500 to about 370–390 they are ready for test. Single-graded doses of "unknown" are administered to groups of such rats (for greatest accuracy, 4 or 5 animals should be included per group) and the heart-rate is measured about twice daily. The time which elapses before the heart has fallen back to the original value at the beginning of the test is noted. Simultaneously graded doses of the international standard are administered to a comparable group of rats and measurements taken in the same manner. (For the sake of accurate standardisation, similar tests have also been made with specimens of pure crystalline vitamin-B_1 hydrochloride obtained from Messrs. Merck; the relation found was—

10γ vitamin-B_1 HCl = 38 mg. of international standard (= 3·8 I.U.).)

Average, or better median, values for each group are then calculated (see Table VI.). A dose-response

TABLE VI

Animal Responses with Crystalline Vitamin B_1 and International Standard

Material.	Dose fed.	Days cured.	
		Individual values.	Average or median.
Vitamin B_1 hydrochloride.	2·5 γ	2, 2, 2, 3	2·2
	5·0 γ	(*a*) 3, 4, 4, 4, 4, 4, 4, 5, 5, 5 / (*b*) 4, 4, 4, 5	4·0
	7·5 γ	5, 5, 7, 7	6·0
	10·0 γ	7, 8, 8, 9, 9	8·0
International standard.	10 mg.	2, 2, 2·5, 3, 3	2·5
	20 ,,	3·5, 4·5, 4·5, 5, 5·5	4·6
	30 ,,	4·5, 5·5, 6, 6, 8	6·0
	40 ,,	6, 7, 7·5, 9, 10	7·9

(*a*) = administered orally. (*b*) = injected subcutaneously.

curve may thus be drawn (Fig. 1), and the dose of the unknown equal in its effect to a given number of units of international standard is thus determined—or the equivalent in terms of so many γ of pure vitamin-B_1 hydrochloride may be given. In approximate routine determinations such lavish use of animals is not called for; 2 or 3 tests per specimen suffices. For fuller details of technique the paper by Birch and Harris [9] may be consulted.

† The use of a simpler oscillograph may furnish a less expensive alternative.

Results

EXCRETION OF VITAMIN B_1 BY NORMAL ADULTS

Typical results for the day-to-day excretion of vitamin B_1 in the urine are shown in Fig. 2 and the averages are summarised in Tables VII. and VIII.

TABLE VII

Daily Excretion of Vitamin B_1 in Urine by Normal Adults

No.	Initials.	Weight in kg.	Age.	Group.	Vitamin B_1 in urine.	
					Conc., I.U. per 100 c.cm. (av.).	I.U. per day (av.).
1	A. W. D.	53	22	1 (M.R.)	0·7	12
2	S. I.	72	25		1·1	13
3	T. W. B.	58	29		1·6	14
4	S. A. C.	67	20		1·2	18
5	L. J. H.	72	37	2 (N.R.)	1·7	21
6	P. C. L.	56	25		1·6	21
7	G. G. G.	71	20		4·2	22
8	V. L.	73	22	3 (G.R.)	3·2	27
9	B. M.	63	17		3·1	35

M.R., N.R., G.R. = moderate, normal, and good reserves.

TABLE VIII

Effect of Single Test Dose Administered to Adults with Varying "Resting Levels"

Group designation.	Initials.	Special features of diet.	"Resting level" before test dose.	Amount of vitamin B_1 excreted, I.U., in one day.	
				After test dose of—	
				340 I.U.	950 I.U.
1. Poor or moderate reserves.	P. C. L.(1)	B_1-free diet for 3 days.	10	11	—
	P. C. L.(2)		11	31*	—
	T. W. B.	Usual diet.	14	—	44
	S. I.	,, ,,	14	26	—
	L. J. H.(1)	,, ,,	15	—	57
	S. A. C.(1)	,, ,,	18	36	—
	V. L.	,, ,,	19	—	46
2. Normal reserves.	L. J. H.(2)	Good diet.	21	68	—
	P. C. L.(3)	,, ,,	21	76	—
	G. G. G.(1)	,, ,,	22	47	59
	P. C. L.(4)	,, ,,	23	67	—
	S. A. C.(2)	,, ,,	25	—	61
3. Good reserves.	B.M.	Diet supp. with 16 g. Bemax daily for 6–12 months.	35, 41	—	66
	S. A. C.(3)	Diet supp. with B_1 concentrate for several days.	37	—	68
	G. G. G.(2)		51	—	199
	S. A. C.(4)		82	—	142

* Previous test doses had been given shortly before.

It will be seen that the subjects have been arranged in three groups roughly classified as "moderate," "normal," and "good." Nos. 1, 2, 3, and 4 (Group 1, Table VII.) are the "moderate" (or poor) group. Their dietary histories indicate a somewhat low intake of vitamin B_1 (the chief source being generally one egg daily and a small amount of milk), and their urinary output is likewise a little below the "normal" (average = 14 international units daily). Subjects Nos. 5, 6, and 7 (Group 2) may be classed as "average" or "normal." Their dietaries include more liberal amounts of milk, brown bread, eggs, &c.; and their average excretion is appreciably higher, about 21 I.U. daily. Two other subjects who had received a diet unusually rich in vitamin B_1 (Nos. 8

and 9, Group 3)—namely, a special daily supplement of 16 g. of Bemax for one year past, plus a good mixed diet, including porridge, bacon, eggs, milk—may be classed as "good"; their average daily excretion was significantly higher again (31 I.U. per day).

It may be concluded, therefore, that an average normal value for the excretion of vitamin B_1 by adult subjects on normal diets in this country is of the order of 20 I.U. per day. The preliminary indications that the output varies according to the dietary intake is confirmed below in a series of carefully controlled observations. We may suppose that the daily excretion varies with the body's "reserves" of the vitamin which in turn depend on the amount provided in the food. Animal tests bear this out. The amount of vitamin B_1 which can be held in store in the body is, however, less important than, for example, in the case of vitamin A, immense reserves of which may be accumulated in the liver.

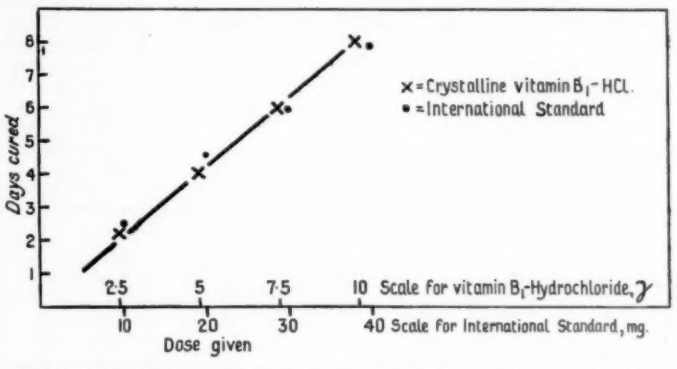

FIG. 1.—Dose-effect curve, for pure crystalline vitamin B_1-hydrochloride and for international standard preparation.

EFFECT OF TEST DOSE

Following the technique described for the determination of vitamin-C subnutrition, we have investigated the effect of the administration of a single large test dose of vitamin B_1. As with vitamin C, we have found that with vitamin B_1 also the effect of the test dose is related to the past dietary history, and hence to the "resting level" of excretion. That is to say, subjects having larger "reserves" of the vitamin and excreting more of it in their day-to-day "resting level" show a somewhat larger immediate response to a given test dose than do those whose past diet has been poorer in the vitamin. Typical values are given in Table VIII.

Reference to Table VIII. suggests that for the diagnosis of the more moderate degrees of vitamin-B_1 subnutrition a suitable level for the test dose is probably about 900γ of vitamin B_1 HCl (=340 I.U.). Such a dose gives a good response with "normal" subjects, and little response from subjects with somewhat subnormal past intakes of the vitamin. On the other hand, the test for subjects with unusually high values for their resting level was

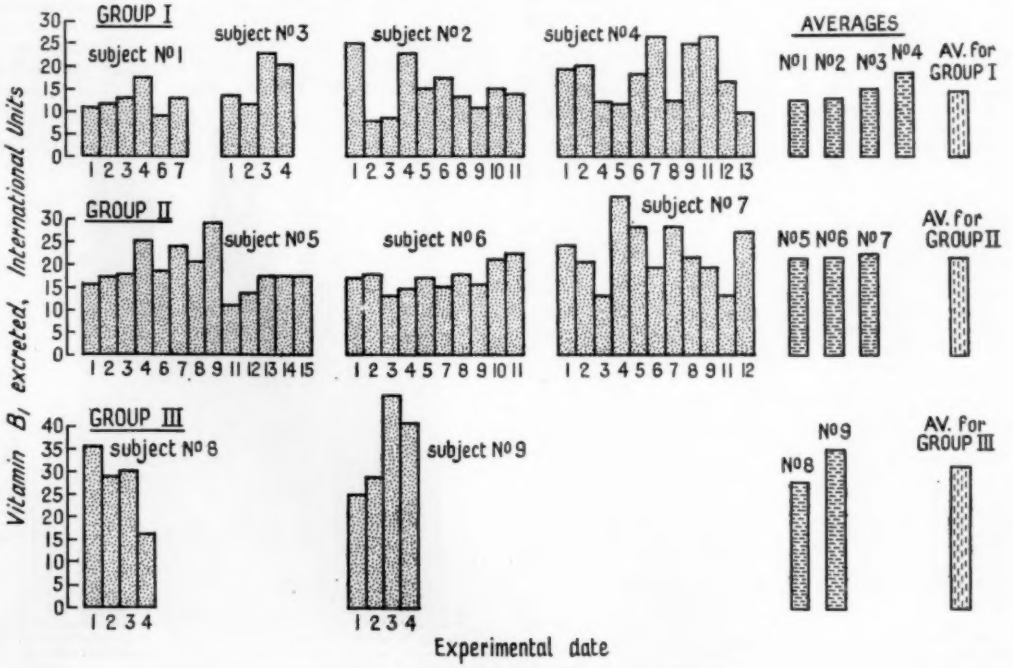

FIG. 2.—Day-to-day excretion of vitamin B_1 by nine adults.

Group I. (Nos. 1–4).—Average resting level = 14 I.U. daily, "moderate reserves."
" II. (Nos. 5–7).— " " " = 21 " " "normal reserves."
" III. (Nos. 8–9).— " " " = 31 " " "good reserves."

made more dramatically evident when a still larger test dose was tried. For example, subjects who had had a diet unusually rich in vitamin B_1 and were excreting it at the high rate of 51–82 I.U. per day, gave a response of no less than 140–200 I.U. after a test dose of 950 I.U.

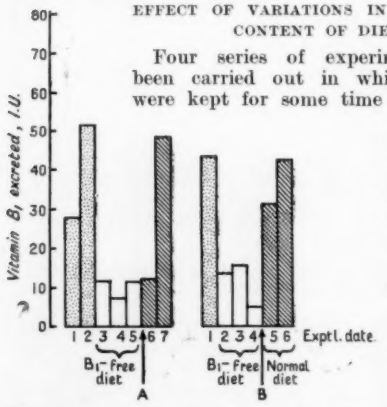

FIG. 3.—Effect of diet free from vitamin B_1 on a subject with good reserves. At A a diet containing about 490 I.U. daily was given. At B a test dose of vitamin B_1 (342 I.U.) was given, followed by normal diet.

EFFECT OF VARIATIONS IN VITAMIN-B_1 CONTENT OF DIET

Four series of experiments have been carried out in which subjects were kept for some time in turn on diets containing varying amounts of vitamin B_1. The results are illustrated in Figs. 3–6. As will be observed, a definite correlation is shown between the vitamin-B_1 intake and the urinary excretion.

(1) Expt. I. (Fig. 3) illustrates the rapid depletion of reserves which occurs when a diet is taken containing no vitamin B_1.

A normal subject with a good dietary history was placed for 3 days on a B_1-free diet, consisting mainly of polished rice, cream crackers, egg-white, and butter. His excretion of vitamin B_1 quickly fell from an initial value of 51 I.U. per day to the subnormal value of 10 I.U. On the fourth day foodstuffs rich in vitamin B_1 were restored to his dietary (eggs, milk, pork, bacon, green vegetables; calculated to contain a total of about 490 I.U. of vitamin B_1), yet his output remained for a time subnormal. This clearly indicated that a considerable depletion of the vitamin-B_1 reserves had occurred and that the vitamin B_1 consumed on the fourth day was utilised in "saturating" the tissues once again to their previous level. On the following day the excretion had returned to the original normal value. A few days later the experiment was repeated and a similar result obtained. After three days on the B_1-deficient diet the test dose of 342 I.U. gave only about one half of the response obtained with a normal subject.

(2) Expt. II. (Fig. 4) illustrates results obtained with a subject having an initial low "resting level," his previous dietary history indicating a less than average intake of vitamin B_1. As the amount of vitamin B_1 administered daily was increased from time to time there was a corresponding slow increase in the output. Perhaps the most interesting feature of the results however was that there was some lag in the increased urinary output following upon the increased intake. This would indicate that when the vitamin-B_1 reserves are originally low some of the extra vitamin B_1 administered is first absorbed to "saturate" the tissues up to the new level.

(3) Experiments with a normal subject having a higher initial "resting level" are shown in Fig. 5. The results indicate that with a normal adult having good vitamin-B_1 reserves, the tissues become more rapidly "saturated" after a test dose and a more prompt response is seen in the urinary rise.

(4) A further experiment giving quantitative data for the excretion of vitamin B_1 by a normal subject given in turn various levels of vitamin-B_1 intake are recorded in Fig. 6.

QUANTITATIVE RELATION BETWEEN DIETARY INTAKE AND URINARY OUTPUT ("RESTING LEVEL")

Our results indicate that under normal circumstances only a relatively small amount of the vitamin B_1 taken in the food is excreted in the urine. The proportion excreted is notably less than that for vitamin C, under comparable conditions.[2 3]

An attempt to show quantitatively the relation between the vitamin intake and the output is made in Table IX. For this purpose we have made an allowance of 250 I.U. per day to represent the amount of vitamin B_1 found in the ordinary middle-class dietary. This figure was arrived at from calculations based on the vitamin-B_1 values of foodstuffs as determined by the "bradycardia" method and recently published by Baker and Wright.[10] According to our calculations (cf. below, Table XII.) the vitamin-

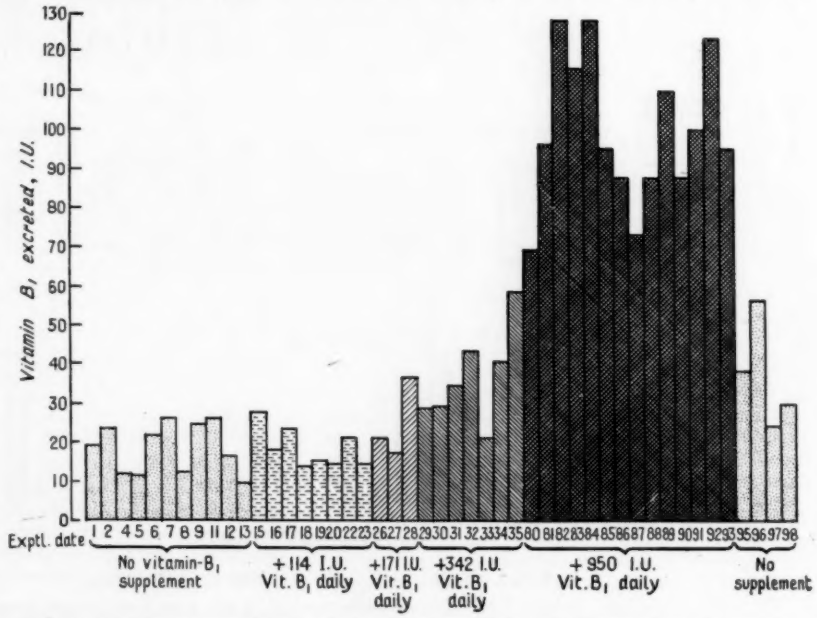

FIG. 4.—Effect of increase in intake of vitamin B_1 in subject with initially rather low reserves.

TABLE IX

Relation between Dietary Intake and Urinary Excretion of Vitamin B_1

Daily dose of vitamin B_1, I.U.	Approx. vitamin B_1 content of diet, I.U.	Total daily intake, I.U.	Average daily output of vitamin, I.U.*	Output expressed as percentage of intake.
As Bemax—				
110	250	360	19 (6)	5
170	250	420	24 (3)	6
170	250	420	27 (4)	6
170	250	420	35 (4)	8
340	250	590	30 (8)	5
As B_1-concentrate—				
500	250	750	34 (2)	5
500	250	750	50 (3)	7
500	250	750	40 (3)	5
1000	250	1250	44 (3)	4
1000	250	1250	100 (10)	8
1000	250	1250	68 (6)	5

* Based on observations for number of days shown in parentheses.

B_1 values of normal dietaries vary from a value of about 200 I.U. for a better working-class regimen (in which the day's food contains moderate allowances of meat, egg, potatoes, and vegetables plus half a pint of milk) to a value of about 400 to 500 I.U. for a richer menu (containing larger allowances of eggs, bacon, potatoes, vegetables, plus one pint of milk). Such an allowance (250 I.U. per day) is clearly no more than a first approximation only, but it serves our present purpose sufficiently well.

Our results are plotted in Fig. 7 and it will be seen that there is a well-defined proportionality between the daily intake and the output of vitamin B_1

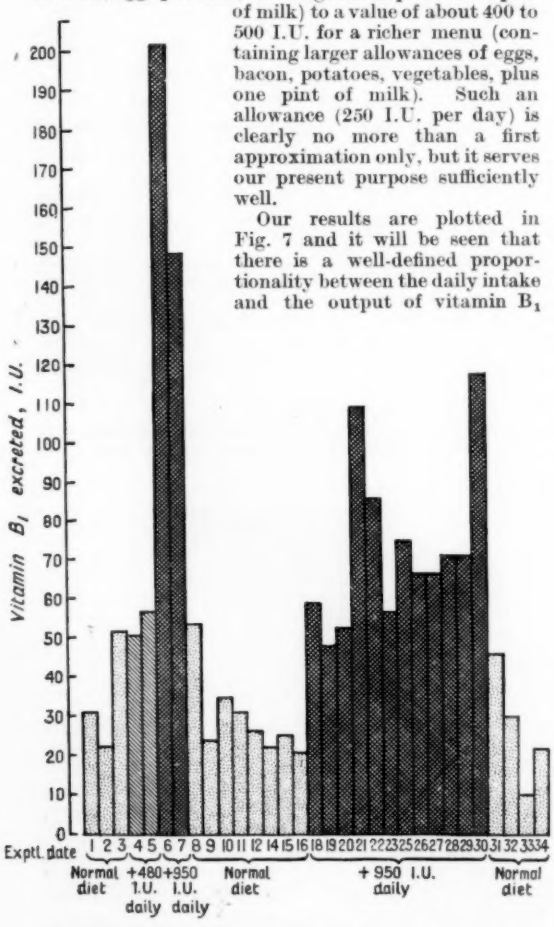

FIG. 5.—Effect of variations in vitamin-B_1 intake. Normal subject.

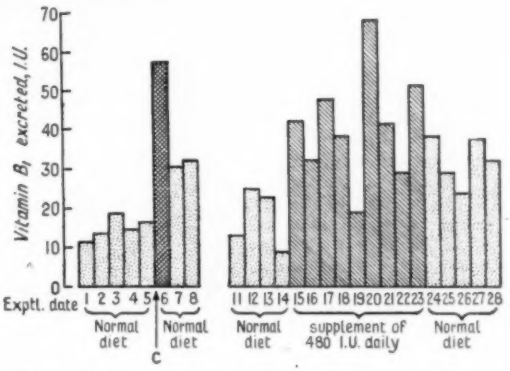

FIG. 6.—Variations in vitamin-B_1 excretion with intake. At C a test dose of 950 I.U. was given.

when a steady state has been reached.† The amount of vitamin B_1 excreted remains fairly constant at around 5 to 8 per cent. of the intake, notwithstanding the wide variations of the latter. As already hinted, this behaviour is rather in contrast with that noted for vitamin C. With vitamin C any very large increase in the intake causes a rapid

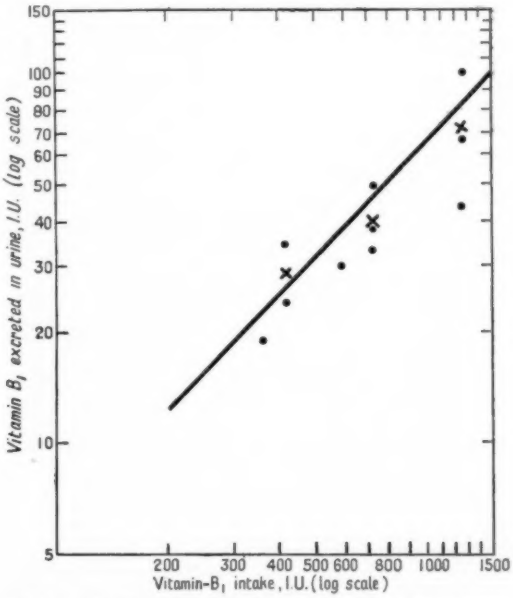

FIG. 7.—Excretion of vitamin B_1 with varying intakes. (Crosses represent averages of groups.)

rise in the output; the tissues quickly become "saturated"; and before long the greater part of the extra vitamin ingested will be excreted—instead of generally only about 5 to 8 per cent. of it as with vitamin B_1.

† It is important to realise that in this section we are referring to the steady state of excretion after equilibrium has been attained on a given fixed daily dose of the vitamin continued for some time—i.e., when "saturation" has been reached for the given level of intake. Obviously the more *immediate response* seen just after a change has been brought about in the vitamin intake—as when a test dose is given—depends on the past vitamin history, that is, on the state of the body's reserves.

It is reasonable to assume that vitamin B_1, being water-soluble, is readily absorbed and distributed by the blood stream, and it appears to be quickly eliminated by the kidneys. Thus we found in one experiment that the administration to a normal subject of a test dose of 950 I.U. led to the excretion of about 90 I.U. after 2 hours—that is, about 9 per cent. of the dose given.

We may therefore conclude that in the metabolism of vitamin B_1 by the normal human body, about 5 to 8 per cent. of the vitamin is quickly eliminated unchanged by the kidneys, and that (apart from any lost in the fæces) a greater part of the remainder is presumably destroyed by metabolic changes in the tissues, the exact mechanism of the latter being still obscure.‡

TABLE X.

Excretion of Vitamin B_1 in Urine by Infants and Children

Initials (and sex).	Age years.	Diagnosis.	Exptl. date.	Vol. of urine c.cm.	Vitamin B_1 in urine.	
					Daily total, I.U.	Conc., I.U. per 100 c.cm.
D. C. (m.)	1	..	1	260	4·9	1·9
*J. H. (m.)	3	Convalescence after pertussis.	1	350	4·7	1·3
			2	500	11·8	2·4
			3	500	4·7	0·9
			4	350	9·5	2·7
			av.	..	7·7	1·8
S. N. (f.)	3	Inguinal hernia.	1	335	5·3	1·6
			2	250	4·9	1·9
			3	370	3·8	1·0
			av.	..	4·7	1·5
E. R. (f.)	4	Otitis media.	1	290	5·7	2·0
			2	380	3·8	1·0
			3	440	6·5	1·5
			av.	..	5·3	1·5
G. W. (f.)	5	Broncho-pneumonia.	1	450	4·2	0·9
			2	340	4·9	1·4
			3	510	7·2	1·4
			av.	..	5·4	1·2
*M. B. H. (m.)	6	Convalescence after pertussis.	1	1560	17·2	1·2
			2	800	15·2	1·9
			3	550	5·2	1·0
			4	700	13·3	1·9
			av.	..	12·8	1·5
E. D. (m.)	7	Fractured femur.	1	230	5·3	2·3
			2	385	1·9	0·5
			3	275	5·3	1·9
			av.	..	4·7	1·6
L. H. (m.)	8	Hæmophilia.	1	305	6·8	2·2
			2	830	8·0	1·0
			3	710	6·8	1·0
			av.	..	7·2	1·4
B. C. (f.)	8	Mastoiditis.	1	590	5·7	1·0
			2	275	6·8	2·5
			3	335	7·6	2·3
			av.	..	6·7	1·9

* All subjects except these two were working-class children. The higher daily totals shown by these two compared with other children of the same age is probably significant; they are the children of a nutritional research-worker and had received a diet containing more than the usual working-class allowance of vitamin B_1—including brown bread, Marmite, and ample milk.

LOW VITAMIN-B_1 RESERVES IN DISEASE OR ON SPECIAL DIETS

As a result of a survey of hospital patients which has been begun, a number of cases of low vitamin-B_1 excretion has come to our notice. Three examples may be cited here.

CASE 1.—Aged 72, suffering from carcinoma of the œsophagus, could eat little solid food, and at the time of examination had been on a "light hospital diet" for three days containing little vitamin B_1. His daily excretion of vitamin B_1 was only 4 I.U. per day.

CASE 2.—Aged 41, suffering from general malnutrition, had a daily output of only 2 I.U. He was examined four and five days after admission during which time he had been on "normal hospital diet."

CASE 3.—Aged 60, suffering from bronchiectasis, and on a "normal hospital diet" for four days excreted only 7 I.U. daily (av.).

It is possible that in certain diseased conditions the absorption of vitamin B_1 from the food is interfered with. Further experiments are also in progress to determine how far lower reserves of vitamin B_1 are common in old age.

DATA FOR CHILDREN

Analyses for vitamin B_1 have been carried out on the urine from a number of infants and children. The results so far obtained indicate that the average values for the concentration of the vitamin in the urine is similar to that for adults—viz., about 1 to 2 I.U. per 100 c.cm. The average total daily outputs, calculated on the basis of kilogramme body-weight, is also of the same order as for adults or perhaps rather higher for the better nourished children. (See Table X.)

EXPERIMENTS WITH LABORATORY ANIMALS

As the more extreme degrees of vitamin-B_1 deprivation can rarely be seen in this country, and such deficiency as does exist is probably nothing more than a moderate degree of hypovitaminosis (see below), we thought it would be instructive to determine the effects upon rats not only of partial deficiencies but also of a more established condition of avitaminosis.

Our tests have led to the important finding that in vitamin-B_1 deficiency in the rat the amount of vitamin B_1 excreted in the urine becomes negligibly

TABLE XI

Urinary Excretion of Vitamin B_1 with Varied Allowances of the Vitamin added to Diets of Rats Suffering from hypovitaminosis B_1.

Rat No.	Dose of vitamin B_1 added per day to diet of depleted rat, I.U.	Period during which the vitamin B_1 supplement was administered (days).	Period elapsing after discontinuation of vitamin supplement.	Amount of vitamin B_1 found in the rat's urine, I.U. per day.
1	120	11	1	10
			2	12
2	76	1	7	2
3	19	1	1	1·4
			2	0·7 (*a*)
			3	
			4	0·3 (*a*)
			5	
4	0·6	1	1–5	0·1 (*b*)
	0·2	1	1–5	<0·1 (*b*)
	0·2	1	1–5	<0·1 (*b*)
5	0·15	1	1–5	<0·1 (*b*)
6	0·2	1	1–5	<0·1 (*b*)

(*a*), (*b*) Urine was collected for 2 or 5 successive days respectively, and pooled in order to obtain enough for an estimation of the vitamin-B_1 content.

Note.—Rats 5 and 6 were suffering from a more advanced state of deficiency, and rat 4 from a gradually increasing degree of hypovitaminosis.

‡ Apparently little of the vitamin B_1 of the food is lost in the fæces. The antineuritic potency of the latter is due to the presence of micro-organisms and bears little or no direct relation to the amount of vitamin B_1 in the diet (unpublished data).

small and indeed is scarcely possible of detection (Table XI., rats 4–6).

Furthermore, the experiments on rats confirm the two principal conclusions reached in the tests on human beings: (1) The vitamin-B_1 output varies according to the amount given in the diet (Table XI., rats 1–4). (2) The amount excreted is a small fraction only of that ingested—namely, about 8 per cent., when the steady state has been reached (that is the same fraction as for human beings). (Rat 1, Table XI.)

Discussion

Having shown that the subject's dietary history determines his excretion of vitamin B_1, as also his response to a test dose, the next thing to consider is how these results may be turned to use in relation to problems of human dietetics, as for the determination of the prevalence of undernutrition and for the establishment of vitamin-B_1 standards. Surveys are at present in progress in which our object is to determine average values for excretion in different sections of the community, and to correlate these with the consumption of diets believed to contain either adequate or inadequate amounts of vitamin B_1. A considerable amount of large-scale experimental work, carried out mainly in America,[11] goes to suggest that a suboptimal intake of vitamin B_1 is not uncommon, especially in bottle-fed babies, for when extra sources of the vitamin (generally of cereal origin) were added to the diet the growth-rates and weight curves went far ahead of those of the control groups. An immediate need therefore is

TABLE XII

Calculated Vitamin-B_1 Content of Representative Normal Diets, Cambridge, 1936

Subject.	Description.	Day.	Amount of vitamin B_1 I.U. per day.
G. G. G.	Laboratory assistant.	1	167
		2	142
		3	361
		4	221
			av. 223
S. A. C.	,,	1	410
		2	256
		3	234
		4	234
		5	291
			av. 285
P. C. L.	Research worker.	1	410
		2	498
		3	508
			av. 472
L. J. H.	,,	1	290
		2	360
		3	330
		4	510
			av. 470

that such observations be correlated with the corresponding values for urinary excretion of vitamin B_1 on the different diets. It may be added that as far as adults are concerned there is also reason to suppose that large numbers of unemployed and poorer-paid workers, subsisting on diets consisting largely of white bread, margarine, jam, tea, sugar, condensed milk, potatoes, &c.,[12] are likely to be below the optimum in their intake of vitamin B_1.

Judging from our own short-time experiments on B_1-free diets, as well as from the experiments on avitaminous rats, there seems little doubt that in a state of advanced deficiency of the vitamin (i.e., in beri-beri) vitamin B_1 will cease to be excreted in any significant amount. Indeed, preliminary observations (made possible by the kind help of Prof. J. L. Rosedale) showed that in 7 cases of beri-beri no appreciable amount of vitamin B_1 was being excreted in the urine (viz., $< 2{\cdot}5$ I.U. per day), although the patients had already been placed for treatment on B_1-rich diets. The urine test therefore promises to be of diagnostic use in this connexion, and we hope to publish further data on this aspect of the problem in a later communication. As a simple alternative to the test-dose technique, measurements may be made of the amount of vitamin B_1 excreted during a period of 24 hours while the subject is temporarily restricted to an experimental diet containing no vitamin B_1. Well-nourished controls are found to carry sufficient "reserves" of the vitamin to be able to continued to excrete significant amounts of it in their urine under these circumstances (see Fig. 3).

TABLE XIII

*Calculation of Vitamin-B_1 Needs of Human Beings**

No.	Description of diet.	Calculated vitamin B_1 content of diet, I.U. per day. Against beri-beri— Diet not protective.	Diet protective.
1	Fletcher, 1905.	152	286
2	Frazer and Stanton, 1907.	130	382
3	Megan and Bhattacharjee, 1924.	200, 206	256, 282
4	"Average" (? liberal) American diet, Sherman, 1924.	..	342
5	Average North China diet, Adolph, 1925.	..	264
6	Institutional diet for school-children (containing 1 pint of milk daily), Corry Mann, 1926.	..	374
7	Average for Cambridge Laboratory assistants (present work: see Table XII.).	..	220–290 (av. 250)

* Nos. 1 to 5 are quoted from Cowgill's "The Vitamin B Requirement of Man," [13] the data being re-calculated on the basis that 1 "mg. equivalent" = 0·05 I.U. No. 6 is from Medical Research Council, Special Report Series No. 105, 1926.

Nutritional standards for vitamin B_1.—It is perhaps not premature to essay a few preliminary calculations in the endeavour to determine the probable minimum (or optimum) needs for vitamin B_1, and the corresponding values for the urinary response. We have estimated the vitamin-B_1 content of a series of characteristic normal diets, and find that an average middle-class (or a better working-class) diet at Cambridge may be expected to contain about 250 to 500 I.U. per day (see Table XII.). A consideration of past clinical records suggests that diets containing less than about 150 to 200 I.U. per day may be inadequate to cure or prevent beri-beri (Table XIII.). Hence a daily intake of 200 I.U. (for a man of 10 st.) may be fixed provisionally as the minimal standard allowance §; and reference to the previous tables given in this paper entitles one to reach the conclusion that if a subject excretes less than about 12 I.U. per day (per 10 st. body-weight—the urine having an average concentration of less than about 1 I.U. per 100 c.cm.) a strong presumption must be raised that his diet contained less than a normal allowance of vitamin B_1.

§ To avoid undue complication, we may ignore the consideration that more precisely the vitamin-B_1 requirements somewhat increase with an enlarged calorific intake or extra carbohydrate.

Summary

In the search to find a simple method of estimating the state of vitamin-B_1 nutrition of human subjects, quantitative studies have been carried out of the day-to-day excretion of vitamin B_1 in the urine. This can be measured simply and rapidly by means of the "bradycardia" method (Harris). It is shown that the output varies with the dietary intake. In a group of 9 healthy adults (aged 17 to 37) on "normal" diets the amount excreted (November to February) was of the order of 12–35 I.U. (= 30–90 γ of vitamin B_1 hydrochloride) with an average of 20 I.U. per day. This represents only a very small proportion (about 5–8 per cent.) of the daily intake of the vitamin (cf. vitamin C). The consumption of a diet containing comparatively small amounts of vitamin B_1 led to a proportional reduction in the daily output of the vitamin, while a diet containing large amounts produced a corresponding increase. The immediate response in excretion after a large test dose of the vitamin was also appreciable graded, according to the past dietary history. Similar results were obtained with experimental animals (rats): in hypovitaminosis-B_1 the amount excreted became negligibly small. Reference is made to preliminary surveys which are in progress to measure the state of vitamin-B_1 nutrition in groups of healthy and diseased children and adults. A daily excretion of less than 12 I.U. (corresponding with an average concentration of 1 I.U. per 100 c.cm.) raises the presumption that the diet contains less than a normal allowance of vitamin B_1. Preliminary observations confirm the expectation that in actually developed avitaminosis (beri-beri) in man vitamin B_1 may cease to be excreted in the urine in appreciable amounts ($< 2{\cdot}5$ I.U. daily).

Our thanks are due to Dr. A. Z. Baker, of Vitamins Ltd., for supplying concentrated preparations of vitamin B_1 and specimens from two human subjects on special diets. Estimations on several pathological subjects were made possible through the valued collaboration of Dr. Leslie Cole and Dr. John Yudkin at Addenbrooke's Hospital, Cambridge.

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DEACONESS HOSPITAL, EDINBURGH.—At the annual general meeting of the Church of Scotland Deaconess Hospital reference was made to the extension and reconstruction of the hospital which is now being carried out. The total alterations involve an expenditure of £40,000, of which £28,000 has already been subscribed. The hospital has been closed since August, 1935, but the district maternity work has been continued. It is hoped that the reconstructed hospital will be reopened in October

GLYCOSURIA AND ACETONURIA IN SUBARACHNOID HÆMORRHAGE

A REPORT OF FOUR CASES

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THE occurrence of hyperglycæmia and glycosuria following cerebral injury has been recognised since Claude Bernard described his experiments of fourth-ventricle puncture in the middle of the last century. As one of the findings in the examination of the urine of patients suffering from hæmorrhage into the subarachnoid space glycosuria is by no means uncommon. When this glycosuria is associated with acetonuria in a comatose patient, it may lead to errors of diagnosis. This possibility has been pointed out by Hinds Howell,[1] but apart from his observation it seems that the condition has attracted little attention in this country. In 1929 Rømcke and Ustvedt[2] described 27 cases of subarachnoid hæmorrhage: in one of these glycosuria and acetonuria were found. In the following year 2 more cases were described, 1 by Bix[3] in Vienna and 1 by Vitkova and Vitek[4] in Paris. Rømcke and Skouge[5] have since described 14 cases of cerebral hæmorrhage and 1 of epilepsy in which acetonuria was demonstrated. More recently 2 further cases have been recorded by Jamieson and Scott[6] in Canada, and 1 by Rathery, Hesse, and Roy[7] in France.

In each of the 4 cases of hæmorrhage into the subarachnoid space described below, acetone and sugar were found in the urine, and 1 presented a clinical picture which resembled in some respects that of hyperglycæmic coma. An examination of the records of St. George's Hospital has revealed 1 other case of proved subarachnoid hæmorrhage in which it is recorded that "a minute trace of acetone" was found in the urine. Since the nature of the test used and the extent of the minute trace of acetone demonstrated are not disclosed, the case is not included in this series. It is of interest, however, to note that this patient was given insulin before the true diagnosis was revealed by lumbar puncture.

CASE RECORDS

CASE 1.—A woman, aged 59, was admitted to St. George's Hospital Dec. 24th, 1933. It was stated that she had suffered from "blood pressure" for some months, but the exact nature of her symptoms was never satisfactorily ascertained. No story could be obtained from relatives in any way suggestive of the symptoms of diabetes mellitus. It was subsequently learnt that her systolic blood pressure had recently been in the neighbourhood of 240 and that the urine was sugar-free a few weeks before admission. On the evening before admission she took a short walk, and on her return sat down in a chair to rest. Here she was discovered by her relatives, who found that they were unable to rouse her. She remained unconscious throughout the night, vomiting from time to time. At 11.30 on the following morning she was admitted to hospital.

On examination she was profoundly unconscious; the temperature was 99·4° F.; pulse-rate 130, regular and of good volume; respiration-rate, 36; blood pressure was 130/80. The breath was excessively foul but free from any odour of acetone; the intra-ocular tension was not abnormal; the tongue was dry and coated, and crusts hung from the lips. The heart was slightly enlarged, the apex-beat being in the fifth space 4 inches from the midline; the sounds were weak and there were no murmurs. Apart from moist râles at both bases the chest was normal. The pupils were slightly dilated and failed to react to light; there was no corneal reflex; the fundal vessels showed some arterio-sclerotic change and the discs were

normal. All tendon reflexes were extremely sluggish and the abdominal and plantar reflexes were not obtained. The urine contained red cells, albumin, sugar by Fehling's and Benedict's tests, and acetone by Rothera's nitroprusside test; the last-named test was strongly positive, but Gerhardt's ferric chloride test was negative. The cerebro-spinal fluid was under a pressure of 230 mm. of fluid and two specimens which were withdrawn consecutively were intimately and equally mixed with blood.

Course.—The patient failed to regain consciousness and died of pulmonary œdema 48 hours after admission. Permission to make a post-mortem examination was refused.

CASE 2.—A woman, aged 29, a domestic servant, was admitted to the hospital Sept. 29th, 1935. For about two years she had suffered from headaches which had become gradually more severe during the last few months; otherwise she had enjoyed good health. There was no history of polyuria, polydipsia, or loss of weight. At 11 o'clock on the night of her admission, while visiting her mother, it is stated that she complained of pain in the back of the neck and said that she felt unwell. She returned to her place of employment and retired to bed. At midnight she rang her bell and was found in a dazed condition from which she rapidly passed to deep coma. There was no history of her having vomited.

On examination at 2.30 A.M. she was found to be deeply unconscious, cold, and clammy. The temperature was 96° F.; the pulse-rate 88, regular, and of good volume; and the respiration-rate 14. The blood pressure was 135/90. There was no odour of acetone in the breath, which had a heavy stale smell. No abnormal physical signs were detected in the heart; there were a few scattered râles on both sides of the chest, but it was otherwise normal. The pupils were small, equal in size, and reacted to light; the optic discs were slightly blurred at the edges; there were no fundal hæmorrhages. The tendon reflexes were present and equal on both sides; there was a bilateral extensor plantar response. The urine was found to contain sugar by Benedict's test, and Rothera's test for acetone was strongly positive; but the ferric chloride test was negative; no other abnormal constituents were found. The cerebro-spinal fluid was under increased pressure which was not measured, and was intimately mixed with fresh blood; two specimens were taken and were found to be of the same degree of coloration.

Course.—The pulse-rate and the temperature rose steadily and the respiration-rate fell to 12. The patient died seven hours after admission without regaining consciousness.

Post mortem the right cerebellar fossa contained about 2 oz. of blood. The upper part of the right lobe of the cerebellum was markedly macerated; the fourth ventricle, the aqueduct of Sylvius, and the lateral ventricles contained blood. Both the aqueduct and the ventricles were somewhat dilated. Stained sections of the cerebellum examined microscopically showed no evidence of tumour or cyst in which the hæmorrhage might have originated. It is probable that the hæmorrhage occurred from the right posterior superior cerebellar artery. No aneurysm, however, was found. The lungs were congested, but otherwise normal. The aorta showed early atheromatous changes. The spleen and kidneys were congested. No abnormality was detected in the other organs.

CASE 3.—A man, aged 43, a car salesman, was admitted to the hospital on Oct. 1st, 1935. His general health had been poor for two years during which time he had suffered from lassitude and fits of depression. Three weeks before admission he had had an attack of numbness in the left arm which had passed off after a few hours. For five days he had complained of headache which had become progressively worse. There had been no history of an abnormality of thirst, appetite, or micturition. On the evening of his admission to hospital he had consumed a large meal. While resting after this meal he suddenly collapsed and, after remaining inert for a few moments, became extremely violent and noisy. He did not vomit.

On examination he was found to be quite irrational. During the course of the clinical examination morphine hydrochloride gr. ¼ was given, and before it had been completed he had passed into coma. He vomited once during the examination. The temperature was 95° F., the pulse-rate 80, and the respiration-rate 24; blood pressure was 110/65. There was no odour of acetone in the breath; the tongue was clean. The apex-beat was in the fifth space 3¾ inches from the midline, the sounds were distant, and there were frequent extrasystoles. No abnormality was found in the lungs. The pupils were somewhat dilated and reacted to light; the right fundus only was clearly seen and appeared normal. The tendon-jerks in both arms were very much increased, but were equal on the two sides. The knee- and ankle-jerks on the left were distinctly brisker than those on the right. The plantar response on the left was extensor, that on the right could not be elicited. The abdominal reflexes were present. The urine was found to contain sugar in considerable quantity by both Fehling's and Benedict's tests; Rothera's test for acetone was strongly positive, but the ferric chloride test was negative. The cerebro-spinal fluid had the appearance of pure blood and was under such pressure that a reading could not be obtained with the ordinary manometer measuring up to 300 mm.

Course.—Coma continued to deepen, respiration became more stertorous, and the rate fell to 12 per minute. The pulse-rate remained steady and became regular, but the volume became gradually less. The abdominal reflexes disappeared and an extensor plantar response was elicited on the right side before death occurred 6¾ hours after admission and 7½ hours after the ictus.

Post mortem the surface of the cerebral hemispheres was covered by fresh blood which filled the cranial fossæ and had penetrated to the cerebral ventricles. The hæmorrhage had originated from the left middle cerebral artery in the fissure of Sylvius, where there was considerable destruction of brain tissue. Sections of the cerebral cortex in the immediate neighbourhood of the hæmorrhage showed a marked excess of polymorphonuclear leucocytes in some of the vessels. No aneurysm was found on the middle cerebral artery itself, examination of which was difficult because its remains were embedded in clot to which they were adherent. There were a few petechial hæmorrhages into the duodenal mucous membrane. The lungs, spleen, and kidneys were congested. The heart and other organs were normal.

CASE 4.—A man, aged 59, a silver cleaner, was admitted to hospital on Nov. 15th, 1935. Nothing is known of his past medical history for he lived in lodgings and was without friends. It is probable that he suffered from headaches, since his urine was found to contain salicylates. On the day of admission he was found by his landlady lying in bed in a comatose condition from which she was unable to rouse him. There was no evidence of his having vomited.

On examination the patient was deeply unconscious; he appeared well nourished. The temperature was 97·8° F.; the pulse-rate 56, regular and of fair volume; respiration was stertorous, the rate 40. Blood pressure was 160/80. The area of cardiac dullness was normal and the heart sounds so distant as to be practically inaudible. Moist râles were heard all over the chest, which was otherwise normal. The pupils were fixed and unequal, the left being dilated and the right constricted. The fundus of the left eye only was seen; papillœdema was present, but there were no hæmorrhages. The tendon-jerks in the arms and legs were present, equal on the two sides and not exaggerated. The abdominal reflexes were absent; a bilateral extensor plantar response was obtained. The urine contained much albumin; Benedict's test for sugar was strongly positive and an immediate strongly positive reaction was obtained with Rothera's test, but the result of the ferric chloride test was obscured by the presence of salicylates. The cerebro-spinal fluid was under increased pressure, which was not measured, and was deeply and uniformly stained with fresh blood.

Course.—The patient died without regaining consciousness three hours after admission, and four hours after he had been found to be in coma.

Post mortem the seat of the hæmorrhage was found to be in the anterior part of the right parietal lobe. Here there was a cavity containing macerated brain substance and blood clot, which had ruptured into the lateral ventricle. Both lateral ventricles, the third and the fourth ventricles, contained blood. From the fourth ventricle sufficient blood had leaked to produce large collections at the base of the brain and beneath the arachnoid on the surface of

the cerebral hemispheres. There was early atheroma of the aorta, the heart was somewhat fatty, the kidneys and spleen were congested, the lungs œdematous, and the liver fatty.

DISCUSSION

Apart from the fact that sugar and acetone were demonstrated in the urine, and that all four illnesses were fatal, these cases have little in common. In the three in which a post-mortem examination was made the only common findings were extensive destruction of brain substance and the presence of blood or deeply blood-stained fluid in the cerebral ventricles; the site of the hæmorrhage was different in each case. It is interesting to note that the findings in Case 3 were almost identical with those described by Jamieson and Scott [6] in their second case. Case 1 was sent to hospital with the diagnosis of diabetic coma, having been seen by her own doctor; the true nature of the condition was revealed by lumbar puncture which was performed chiefly in view of the absence of acetone in the breath and the negative Gerhardt's test. The presence of a strongly positive Rothera's test was, at the time, thought to be due to the patient having taken no food for some 18 hours and during that time she had vomited frequently. In Cases 2, 3, and 4, however, there was no emesis before admission, and in two of them the urine was examined within three hours of the ictus. In Case 3 the patient had recently taken a large meal. It seems, therefore, that the ketonuria is not the result of starvation.

The possibility that these patients were the subjects of undiagnosed diabetes mellitus cannot be excluded. There is no evidence in support of such a conjecture, except for the history of lassitude in Case 3. It is known that the urine of Case 1 had been sugar-free a few weeks before her final illness. In the case described by Bix [3] and three of those recorded by Rømcke and Skouge [5] the patients were known to be non-diabetics.

The urine in each was obtained by catheterisation. The lubricant and the disinfectants used have been shown to contain no acetone either as part of their composition or as an impurity. The tests were Rothera's nitroprusside test and Gerhardt's ferric chloride test. In each specimen the former was strongly positive; a deep purple coloration developed almost immediately and rendered the solution opaque within the space of a few minutes. The ferric chloride test was negative in three cases and indefinite in one. It therefore seems probable that ketone bodies occurred in the urine in small quantities only; acetone alone may have been present, but that is extremely improbable.

The mechanism whereby ketonuria is produced in these cases is obscure. It seems that the hyperglycæmia following either piqûre or pathological cerebral injury is the result of sympathetic stimulation. According to Macleod [8] and others, glycogen is liberated from the liver as the result of stimuli reaching that organ through the hepatic nerves, reinforced by the action of adrenaline, increased secretion of which occurs following stimulation of the suprarenals through the splanchnic nerves. Hubbard and Wright [9] have shown that the injection of adrenaline in healthy individuals produces a definite rise in the quantity of ketone bodies in the blood. It is possible therefore that the ketonuria is the result of a massive increase in the secretion of adrenaline. An alternative theory involves the assumption that there is pancreatic dysfunction as the result of deranged nervous control. It has been shown by Clark [10] that the islets of Langerhans normally receive inhibitory stimuli through the vagi. If the centres of origin of such stimuli were themselves stimulated as the result of hæmorrhage a true diabetes might result.

Bix [3] objects to theories suggesting central causation of ketonuria on the grounds that it has not been produced by piqûre. The stimulus acting upon a cerebral centre following an intracranial vascular catastrophe is associated with sustained increased pressure, and is of a very different order from the temporary stimulus of experimental piqûre. It is difficult therefore to uphold his argument.

One of the cases recorded by Rømcke and Skouge [5] showed a positive test for acetone while the tests for sugar were negative. This would seem to oppose both the theories outlined above, although as these authors point out, in a patient with small glycogen reserves the hyperglycæmia would be of mild degree and short duration. Both theories involve the acceptance of views and experimental work concerning which there is some dispute.

Be the explanation of the ketonuria what it may, it is in the difficulty of diagnosis to which it may give rise that the real interest lies. The coma following intracranial hæmorrhage may, in the absence of signs directing the attention to the central nervous system, simulate the coma of hyperglycæmia so closely that differentiation of the two conditions may be extremely difficult. It is unusual for the odour of acetone to appear in the breath following subarachnoid hæmorrhage, but its presence has been described.[4] In none of the cases recorded has altered intra-ocular tension been found. A negative ferric chloride test is common in these cases and, since it must be extremely rare in hyperglycæmic coma, it is valuable in differentiating the two conditions. The test was, however, found to be positive in four of the cases described by Rømcke and Skouge.[5]

SUMMARY

Four cases of hæmorrhage into the subarachnoid space are reported associated with glycosuria. In all of these ketone bodies were present in the urine in small but definite amounts, as evidenced by a strongly positive Rothera's test. The differential diagnosis from diabetic coma can be made in the absence of neurological signs by the ferric chloride reaction, which is usually negative in subarachnoid hæmorrhage; in diabetes it is almost always positive. In each patient there was extensive destruction of brain substance and the ventricles were filled with blood. It was not possible to determine whether the ketonuria was due to sympathetic stimulation, causing an excessive secretion of adrenaline, or to pancreatic dysfunction due to central irritation.

I am indebted to Dr. Anthony Feiling and Dr. Hugh Gainsborough, under whose care these patients were admitted, for permission to publish the cases, to Dr. John Taylor and Mr. Garthowen Williams for the pathological reports, and to Dr. Winterstein-Gillespie for his assistance in translating the German references.

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CLINICAL AND LABORATORY NOTES

A CLAMP FOR STRETCHING CONGENITAL CLUB-FEET

By M. Forrester-Brown, M.S., M.D. Lond.

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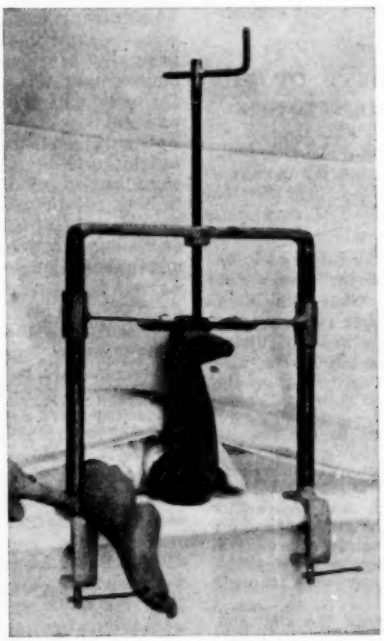
One of the difficulties in correcting the equinus deformity of a congenital club-foot is that, at the age when treatment is most advisable—i.e., in early infancy—the bones are very small and relatively soft in comparison with the dense shortened ligaments. It is therefore essential to localise very accurately the correcting force. In order to get a true dorsiflexion of the ankle, and not merely a pseudo-correction by lifting up the front of the foot at the mid-tarsal region, one must push up the front of the os calcis at the same time that one brings down its posterior end with the insertion of the tendo Achillis, thus restoring the normal tilt to its axis, which in club-foot is horizontal instead of upwards and forwards.

Some surgeons have stated that this manœuvre can only be accomplished by pulling downward with a pin passed deep to the tendo Achillis. I have found, however, that the clamp here illustrated is equally effective. It leaves the surgeon's hands free to control the lateral movements of the foot, so that after dorsiflexion in inversion, which is relatively easy, the foot can be stretched into valgus; for, unlike the contractures of the tendo Achillis in other conditions, that in club-foot is tightest in the everted position, owing to a lateral displacement of the tendon.



The clamp in use.

In an infant whose club-foot is not yielding to regular manual stretching followed by fixation with adhesive strapping (to include the flexed knee), it is best to anæsthetise the child deeply. He is placed prone, in which position the knee is best kept free from lateral strain, and the lower leg lies vertically with the sole upward in the clamp; this is made on the same principle as those used by book-binders. A small cushion should be placed under the knee to protect the patella from bruising and the foot should be steadied so that the cross-bar of the clamp, which is convex downward, fits into the hollow just in front of the os calcis (mid-tarsal joint). While the surgeon steadies the foot, an assistant tightens the screw slowly, gradually forcing the front of the os calcis toward the table, the bone acting as a lever to bring the insertion of the tendo Achillis further from the calf. It is the slow and even stretching afforded by the clamp that is so valuable, as the surgeon's thumb is apt to tire and act unevenly when used for a similar purpose. When used slowly, there is no bruising by the clamp nor tearing of the muscle. If it is found that there is no appreciable stretching of the tendon, as happens in the worst cases, it is desirable to tenotomise the posterior ligaments of the ankle deep to the tendo Achillis; often the external and occasionally, also, the internal lateral ligament should be divided at the same time, though, contrary to what one might expect with a varus deformity, it is the posterior fasciculus of the external ligament, rather than the internal, that obstructs dorsiflexion. The foot should be removed from the clamp for the tenotomy and then replaced, while the surgeon keeps pressure on a dressing over the tenotomy opening. This bleeds briskly for a short time, but if the tenotome has been kept close to the bone the vessels that it divides do not jeopardise the circulation to the foot. After the ligaments are cut, the tendon is fairly easy to stretch, as one's force affects the elastic fleshy belly, which previously had been splinted by the ligaments. The advantage of not tenotomising the tendon itself is that it is always poorly developed in the worst cases of club-foot, the very ones which require manipulation under an anæsthetic, so that there is serious risk of weakening it by immediate correction after division, or by too early stretching of the scar, and it must be remembered that a calcaneus is a more disabling deformity than an equinus. If time is allowed for the divided tendon to reunite the ligaments are also reuniting. Accordingly, I have found this method of dividing ligaments and simultaneously merely stretching the muscles a very valuable one. I have never failed to get full correction of all the elements of the club-foot deformity. This is not the same thing as saying that relapse may not occur later. As I have pointed out in a recent investigation of a large number of late results,[1] the bad club-foot represents not a fixed deformity like that after a badly set fracture but an impetus to faulty development, to resist which will tax all the surgeon's patience and ingenuity during the whole period of the child's growth.

As soon as the foot falls limply into the corrected position it is removed from the clamp and enclosed in plaster with the knee at right angles and the child still prone. Stockingette is applied and three pads only are inserted under it—i.e., one on the dorsum of the foot, one over the tendo Achillis, and one over the patella. Heussner's glue is then poured over the heel to prevent the ill-developed heel slipping upward and plaster is applied directly over the stockingette, very smoothly without any dragging. It is essential to mould closely, as these feet slip very

[1] Jour. Bone and Joint Surg., 1935, xvii., 661.

easily and then get sore; as an index of this it is useful to mark with an indelible pencil the line of the toes when the plaster is finished, when any slipping upward is noticeable at once. If the patient is going into the country, one may split the plaster up the dorsum so that it could be easily removed if serious disturbance of the circulation occurred. The bad cases have shortening of the vessels and nerves behind the ankle, as well as of the other tissues, and poor circulation is the rule. Nevertheless, with the technique described and fixation of the knee in flexion, which relaxes the popliteal vessels, no serious trouble has been encountered. In the worst cases, in which open operation has been necessary in older children, it has been noted that when the obstructions to dorsiflexion have been dealt with and the foot brought to a right angle with the leg, not only is the astragalus incongruous to the tibia, but the circulation in the foot ceased until the angle was altered to about 100°, at which point blood again flowed into the stretched posterior tibial artery. It is not clear why the relaxed anterior tibial vessels do not suffice.

SUPPURATING DERMOID CYST OF THE GASTROHEPATIC OMENTUM

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OMENTAL dermoids are amongst the rarest of intraperitoneal lesions. Shapiro and Meyer [1] were able to find records of 33 cases, other than their own. I have been able to collect five further references.[2-6] Although dermoids and teratomata are ubiquitous in distribution, the cases of Shapiro and Meyer, and of Kowalczyk were the first such growths of the lesser omentum to be recorded.

A boy, aged 7 years, was admitted to the Galway Central Hospital with a history of abdominal pain and vomiting of two weeks' duration; the pain had increased in intensity until admission. He had a temperature of 103° F. (axillary), a pulse-rate of 138, and respiration-rate of 44. The abdomen was distended, rigid, and tender; the tenderness and rigidity were most marked on the right side, the maximum point of tenderness being about 2 in. above McBurney's point, and they were enough to prevent a satisfactory examination.

With a diagnosis of "acute abdomen," the abdomen was opened under ether anæsthesia by a right paramedian incision through the rectus, centred on the umbilicus. There was a little serous fluid in the peritoneal cavity. The cæcum and appendix were normal. A firm œdematous tumour was felt in the right hypochondrium. A few recent adhesions between the anterior abdominal wall and the tumour were divided, and a tense, spherical mass about the size of a cricket ball was delivered through the wound. This was dissected free from the transverse colon, gastrohepatic omentum, and anterior surface of the pylorus, to which it was attached; it seemed to have originated in the lesser omentum above the pylorus. The peritoneum over the tumour and the adjacent structures all showed much inflammatory thickening. During removal the cyst was perforated and material flowed out exactly resembling in appearance and smell the mixture of pus and sebum found in the common suppurating sebaceous cysts; this was mopped up and the abdomen closed without drainage.

Convalescence was prolonged by an abscess of the abdominal wall, but was otherwise satisfactory, the patient leaving hospital on the 31st day in excellent general condition. He has since been readmitted with occasional vomiting and a severe secondary anæmia, which required a blood transfusion. Six months after operation he is said to be in good health.

On section the cyst wall was found to consist of an outer layer of dense inflamed connective tissue with an inner lining of granulation tissue, the original lining having apparently been destroyed by the inflammation. Other parts of the mass consisted of inflamed connective tissue of texture varying from myxomatous to fibrous.

The great *rarity* of such cysts is emphasised by Judd.[7] Preoperative diagnosis must of necessity be exceptional; in point of fact the majority of intraperitoneal dermoids have been discovered during the course of laparotomy for some other concurrent or apparent lesion. In some few cases the diagnosis of mesenteric cyst had been considered preoperatively.

The *symptoms* are those of pressure on the stomach, intestine, or biliary tract, or perhaps, in the case of a retroperitoneal dermoid, of pressure on the kidney or ureter, or great vessels—when the condition might simulate an aortic aneurysm. The *signs* will be a tumour, in uncomplicated cases painless, usually smooth, sometimes fluctuant, and of varying though generally considerable mobility. Among the possible *complications*: are (1) inflammation of the cyst; (2) torsion of the omentum, described by Aviles [8]; and (3) acute intestinal obstruction, described by Foucault. Inflammation of such a cyst has seemingly not hitherto been described, though it is a frequent complication of the commoner ovarian dermoids; it was mentioned as a possibility by Meyer and Shapiro. The *treatment* of these tumours is of course excision, when practicable, and, if this is not possible, marsupialisation as performed by Meyer and Shapiro.

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CONGENITAL ABSENCE OF AN UPPER AND LOWER LIMB

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A FEMALE child, aged 4, was brought to me a few months ago. I found that she had total absence of the right upper and lower limbs and of the left fibula and fifth toe. Free, wrinkled skin covered the right shoulder-joint. At the right hip a small pedunculated knob, like an olive, was to be found in the acetabular area; it looked like a toe and was the sole representative of the components of the right lower limb. There was a severe valgus deformity of the left foot and full, passive extension of the left knee was impossible from disuse, and was limited by about 40°.

A skiagram of the right shoulder showed a normal clavicle, a rather overdeveloped acromion, and complete absence of the glenoid. In the right hip the acetabular zone was without any triradiate formation. It is interesting to note the absence of both glenoid and acetabulum. There was a

small bone, exactly like a toe phalanx, in the skin covering the hip. The left fibula was absent, as well as the fifth toe and its metatarsal. The child uses her left upper limb in a normal fashion. There was nothing relevant in the family history.

I suggested an orthopædic boot to correct the valgus and the use of a crutch to enable her to learn to stand up and gain balance. Possibly, later she may be able to walk about, when the knee and valgus deformities have been treated.

MEDICAL SOCIETIES

WEST KENT MEDICO-CHIRURGICAL SOCIETY

A MEETING of this society held on April 3rd, with Dr. J. R. WYLIE, the president, in the chair, was devoted to a debate on the motion that the

Neurotic Patient Should be Treated by His Own Family Doctor

Dr. F. HUDSON EVANS, in proposing, said that most practitioners have several neurotic patients and although it may be said that doctors live partly by them, certainly these patients live entirely on the doctor. In treating them the doctor should remember that there is usually a reason and foundation for their state and the first necessity was a complete physical overhaul; doubtful points should be referred to specialists, and any related defect should first be treated. A disadvantage, however, of specialist treatment for these cases was the hospital attendance and the inevitable contact there with abnormal and sick people. The neurotic patient required to be surrounded by normal people, to have plenty of work and play, and little time to think about himself. An anxiety neurosis could often be dispelled by the buoyant attitude of the doctor; many people had reason to be anxious—perhaps about their business, their domestic affairs, or their legal position—and confided to their doctor troubles which they would not tell to their parson. The doctor should talk their troubles over with them and assist them as far as possible to accept what could not be altered in their position. After an accident the neurotic patient was slow to recover and then often required alternative —carrot and pitchfork—forms of treatment.

The speaker considered that the manic-depressive tended to become worse in mental hospitals but would ultimately get better if adequately treated at home. The general practitioner should remember that patients with anxiety neuroses do not commit suicide, but that it was dangerous to treat a psychosis as a neurosis. His experience of psycho-analysis was only of one case which had ultimately come to a successful issue, but he felt that the time involved and the danger of rousing sleeping dogs were serious drawbacks to this therapy. The family doctor should treat the neurotic patient as one man to another, and although he should make every effort to secure the relatives as allies he should leave them outside when interviewing the patient. He should find out about the patient's way of living and whether he read medical books and health chats; he should reassure the patient throughout his examination and summarise the findings at the end of the interview. In hysteria the symptoms might be produced and cured by suggestion, but the symptoms were the patient's means of escape from a situation; the patient did not thank the doctor for curing him of his symptoms and so returning him to the original situation.

Dr. Evans had found that the most potent remedy for the neurotic patient was severe depletion of the pocket. It made other treatment more effective and inculcated the desire to get well. The doctor's duty was also to reassure these patients and to try to make their lives happier. He felt that such treatment should be undertaken by the family doctor.

Dr. EDWARD GLOVER said that, while formally opposing the motion, he wished to discuss the means of obtaining really competent treatment of the patient rather than the question of who should undertake it. He himself was neither in favour nor against the motion. In favour of it must be said that not only were there cases which should be treated by the family doctor, but, as Dr. Evans had said, neurotic patients always insisted on treating themselves by going to the family doctor. At the other extreme there were cases of pure neurosis the treatment of which demanded specialised training, and it was positively wrong for the family doctor to attempt it. He likened this position to an emergency of major surgery, where, except, say, on a desert island, a doctor would not undertake the treatment unless he had the skilled training and constant practice of the surgeon. Between these extremes there were two intermediate classes where the family doctor might undertake treatment. There were certain forms of special treatment, such as suggestion, hypnosis, and sidetracking, for which there was no recognised training. If the family doctor had a flair for such methods and combined them with common sense and a friendly attitude he should use his skill; but he must also have a good sense of diagnosis or he might relieve a phobia to precipitate an underlying paranoia.

Then there were minor types of neurotic maladjustment which the doctor might treat if he knew a few rules and they were not hard to acquire. The speaker said that in cases of classical hysteria, obsessions, and compulsions, and some sexual difficulties the usual basis of the neurosis was some violent disturbance of the instincts—not necessarily in their immediate satisfaction, but disturbances which may have lasted from infancy and childhood. When a doctor, faced with a neurotic patient, tried to enter into a patient's difficulties, to agree with his view of himself, and to give him the bottle of medicine asked for, the rapport might be good and the treatment successful. This corresponded to the carrot mentioned by Dr. Evans. In this unwitting treatment it was often best if the doctor knew little of psychotherapeutic methods. But if the doctor disagreed with the patient, even though he did not say so and used various devices to hide the disagreement, the rapport often failed and the patient was likely to become worse. It was therefore important for the doctor to know his capacity in this direction. This second type presumably corresponded to Dr. Evans's pitchfork. There were, however, some passive non-resistant cases which liked to be bullied out of their condition; but such formed only a small proportion of all cases.

Dr. Glover considered that the family doctor might help the patient in some neurotic crises where there was some obvious emotional precipitating factor. For instance, if after the death of a father the son developed a guilt neurosis reproducing the father's

illness, the case might clear up with a simple explanation; but if such cases failed to respond specialist treatment was imperative. The doctor's equipment for such cases included common sense and a big personal factor. Advice and admonishment might occasionally be used, but lying, apart from deliberate suggestion, was inexcusable. Politeness was also required, and, as these patients often received little of it, was often very effective. And the doctor had to have a fairly broad understanding of the patient's general make-up.

The speaker then mentioned the family doctor's part in the prevention of neurosis. It was now known that the foundation of neurosis lay in childhood, but unfortunately few doctors had the understanding of a child's mind, possessed by an ordinary ignorant mother of good feeling. For the doctor who had there was enormous scope in assisting children with their fears and repressions. He thought that most family doctors instead of laying down the law to mothers might well have lessons from, say, four or five sensible mothers on neurosis in childhood.

In conclusion Dr. Glover said that although the family doctor could do much for the simple case requiring kindliness and sympathy, expert and highly trained assistance was absolutely essential for cases of pure neurosis. This could not be given by the general practitioner, even if he had the requisite training—partly because he had not sufficient time (the speaker often took two hours over the first interview with his patients) and partly because it was impossible to carry out psychotherapy efficiently for a few hours only of a busy day.

Dr. F. A. BEATTIE seconded the motion; he said that even Dr. Glover had allowed that three-quarters of the neurotic patients should be treated by the family doctor. There was a trend in medicine to-day for the specialist to take over more and more from the general practitioner's province and insistence on specialist treatment for neurotic cases would take half his practice from him. Sir Humphry Rolleston's oration to the society, entitled the Dumping Ground of Neurasthenia, had encouraged him in the treatment he had been carrying out—more especially of the manic-depressive. He considered that patient treatment on the part of the family doctor helped such people through their phases of depression, but it was important to explain the condition to the relatives. He thought that the greater number of neurotic cases, since they were of minor degree, should be treated by their family doctor; only the more severely affected should be passed on to the specialist.

Dr. S. S. LINDSAY defined a neurotic patient as a man who was not well adjusted to his surroundings; when one considered his surroundings one felt that the relatives and friends who pestered and exhorted him also needed treatment, and that he were better treated away from home. Before treatment such patients needed a thorough clinical overhaul, and Dr. Lindsay felt that the general practitioner had neither the time nor the equipment to assure himself that there was nothing organically wrong. Dr. Beattie had asked what would become of the general practitioner if he lost his neurotic patients; he himself would be greatly relieved.

Prof. J. WOLFSCHON (Canford University, San Francisco) considered the treatment of the neurotic patient from the doctor's and the patient's point of view. The doctor used to be poorly equipped for psychotherapy, although he used it unconsciously on every patient he saw. Nowadays students were given instruction in the prevention of neurosis. The neurotic patient was trying to escape from life not because a particular problem had risen up to attack him but because he was born with a latent instability of his nervous system. When relieved of his neurotic symptoms he still retained his own type of being. Neurotic patients liked to talk, but the busy general practitioner usually cut them short, and so lost their rapport. This impatience in listening was driving patients to the quacks and producing in the United States various cults such as osteopathy and Christian Science. He thought that the neurotic patient was seldom frank with his family doctor for fear of information reaching his parents and relatives. The tendency of the age was to too great specialisation.

Dr. HAROLD PRITCHARD said that the general practitioner's great difficulty in dealing with these cases lay in the diagnosis. He felt that if the practitioner had been specially trained he should treat some of his neurotic patients and that it was impossible to do justice to such cases in a general hospital. Once a patient was labelled neurotic the student was liable to overlook him, but as one grew older such details became more interesting. He thought that true neuroses should receive specialist treatment.

Dr. JANET GRAY cited an example of a nurse suffering from a nervous breakdown who rapidly improved on being given more suitable work.

Dr. E. P. CAREY suggested that there should be institutions and a system of after-care, resembling those for the tuberculous patient, for the neurotic.—Dr. W. E. HALLINAN thought that if there were such sanatoria everybody would crowd into them.

Dr. C. E. BOWEN WILLIAMS mentioned that a sensible mother could do much to prevent neurosis by bringing her children up not to expect too much of life. She thought that it was the craving for affection which drove many neurotic patients to their family doctor for understanding and attention.

Dr. H. V. MORLOCK held that as a neurotic patient was not adapted to his surroundings he should not be treated in them.

Dr. C. J. B. BUCHAN said that in his search for a cure outside himself the neurotic patient was liable to leave his doctor. He knew of one woman who had in the same district changed to nine different doctors since the war.

As mention had been made of the unpleasant homes of neurotic patients, Dr. EVANS pointed out that nevertheless the patients were fond of them and were generally happiest there. He felt that these patients required especially to be away from contact with abnormal people. He was distressed to think what a colony of neurotic patients might be like.

Dr. GLOVER agreed that a family doctor had many advantages in treating neurotic patients, but he considered that a true neurosis required the greater skill of the specialist.

The motion was carried by 11 votes to 9.

TRAINING FOR WORK OVERSEA.—A course for the training of women for citizenship oversea will be formally opened by Sir Archibald Weigall at 4 P.M. on May 1st at 17, Carlton House-terrace, London, S.W.1. Particulars may be had from the secretary, Training of Women for Citizenship Oversea, at that address.

REVIEWS AND NOTICES OF BOOKS

Textbook of Gynæcology

By WILFRED SHAW, M.D. Camb., F.R.C.S. Eng., F.C.O.G., Assistant Physician Accoucheur, St. Bartholomew's Hospital. London: J. and A. Churchill Ltd. 1936. Pp. 588. 18*s*.

IN recent years Dr. Wilfred Shaw has made important contributions to the pathology of certain gynæcological conditions, notably ovarian tumours and the physiology and pathology of menstruation. There is evidence here not only of careful and critical research, both pathological and clinical, but of an extensive knowledge of the literature of the subject.

In its general arrangement the book follows orthodox lines. More stress has been placed upon anatomy and physiology than has been customary in recent text-books of gynæcology, because Dr. Shaw believes that future advances are most likely to come from this direction. The histology and pathology of the ovary and endometrium are fully and clearly described, and as lucid an account as our present limited knowledge allows is given of the part played by the various internal secretions in the control of the ovarian and menstrual cycles. The assessment of the importance of uterine displacements in the production of symptoms is admirable, and will provide additional support to teachers who are constantly finding reason to emphasise the harm which may be done, and in the past was often done, by too energetic treatment of what may be a symptomless abnormality. In his discussion of the operation of hysterectomy, Dr. Shaw finds illogical the argument that total hysterectomy should be performed merely because the cervix, if it is conserved, may subsequently become carcinomatous in about 1 in 150 cases. There are certain formidable arguments on the other side.

If any criticism of this work is called for it is that Dr. Shaw has somewhat neglected the psychological aspect of gynæcology. Here more than in any branch of surgery, the mental outlook of the patient and the possible effect thereon of operative or other intervention are of extreme importance. The illustrations merit special notice. There are four plates in colour and nearly 250 figures in the text. Dr. Shaw has gone far afield for his material; he has picked the best he could find at home and abroad and has added original diagrams and microphotographs where required.

This excellent book, which is comprehensive in scope and yet not too bulky for the needs of the medical student, should achieve and hold a recognised position as a text-book.

Treatment of Diabetes Mellitus

Fifth edition. By ELLIOTT P. JOSLIN, M.D. Harvard, Clinical Professor of Medicine, Harvard Medical School. London: Henry Kimpton. 1935. Pp. 620. 28*s*.

IN the fifth edition of his well-known book Prof. Joslin has secured the coöperation of Dr. Root, Dr. White, and Dr. Marble, who have written certain sections. In the discussion on the pathology of diabetes Prof. Houssay's work receives close attention. He has shown that the pituitary gland secretes a hormone which raises the blood-sugar and counters the action of insulin. When the pituitary gland is removed from a dog, and at a later date the whole of the pancreas, the animal does not develop diabetes; but hyperglycæmia and glycosuria can always be produced in these dogs by the injection of a pituitary extract. The exact bearing of this interesting observation on the pathology of diabetes is not yet clear. A noteworthy account of the influence of heredity is given by Priscilla White and R. Pincus. They have studied 2817 siblings and show that the inheritance of diabetes is a recessive character. Even then, at the time the figures were examined, marriage between two diabetics, between a diabetic and a diabetic carrier, and between two diabetic carriers, had led to a smaller percentage of diabetic children than would have been anticipated. Since, however, diabetes is a disease which commonly develops after the age of 40 it is possible that in investigations to be made 30 years hence the figures for the same families will more nearly approach those expected under Mendelian laws of heredity. It is suggested here that the development of diabetes depends primarily upon the transmission of a single recessive gene, but also on the operation of one or more of these secondary factors—obesity, the increased consumption of sugar all over the world, and the reduction in muscular activity associated, among other causes, with the efficiency of machinery. The dietetic requirements of healthy persons are fully discussed, and also the changes which are necessary after the development of diabetes. Prof. Joslin, in his teaching, occupies an intermediate position between the advocates of high and low content of the diet; he favours between 100 g. and 200 g. per day for a patient weighing 144 lb., the average figure of choice being 140–150 g. with protein about 70 g. and fat 50 g. to 100 g. The course and treatment of coma are discussed very fully, and special sections are devoted to gangrene, tuberculosis, and cancer. The food tables are elaborate and would be even more valuable if compiled on the basis of the different amounts of food which contain 5 g. of carbohydrate.

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1. I Knew 3000 Lunatics

By VICTOR R. SMALL, M.D. London: Rich and Cowan Ltd. 1935. Pp. 273. 7*s*. 6*d*.

2. Asylum

By WILLIAM SEABROOK. London: George G. Harrop and Co., Ltd. 1935. Pp. 266. 8*s*. 6*d*.

1. THE number of writers who describe their mental illnesses grows apace. A few of these works are by practised writers who have been patients or by people with a gift for narrative: their accounts are interesting, even when they manifestly distort the occurrences which provide the main attraction of the book for many readers. Other ex-patients, accurate in their recollection and not influenced by residual features of their psychosis, are misled into fine writing, and thus manage to give an unjustified impression of falsehood. That few combine literary skill with a true picture of their own behaviour or of the life in the mental hospital is not astonishing when we remember that a distorted outlook and a faulty adaptation were the reason for their segregation. It is thus with satisfaction that we note that Dr. Small's book is not by a patient but by a psychiatrist. His description of a provincial mental hospital in the United States may be taken as accurate, though his style may not please. He regards the

mental hospital in which he worked for six years as a place in which he was "privileged by fate and fortune to view from many angles the enactment of a complex drama of romance and crime, pathos and dark tragedy," and it is in this strain that he gives a rather pinchbeck account of an experience that was doubtless genuine enough but is hardly made to seem so to the reader.

2. Mr. Seabrook writes plainly and tellingly, and provides here what is probably the best description available of what goes on in a modern mental hospital. The alcoholism for which the author sought treatment did not impair his ability to see what was happening around him and afterwards to report it accurately: he has no paranoid or crusading axe to grind, his attitude is fair, even to the doctor whom he disliked, and his descriptive powers would surely be the envy of the psychiatrists who had to record his condition. The great hospital near New York in which he spent seven months is among the best of its kind in the world. Those who have read only trivial, denunciatory, or psychologising books about the conditions of treatment of the mentally ill can see here what is actually done, its efficacy, and the impression it may make on the patients themselves.

A Textbook of Surgical Pathology

Second edition. By C. F. W. ILLINGWORTH, M.D., F.R.C.S. Edin., and B. M. DICK, M.B., F.R.C.S. Edin., Lecturers in Clinical Surgery, University of Edinburgh. London: J. and A. Churchill Ltd. 1935. Pp. 719. 36*s*.

THE authors have been at pains to bring this text-book up to date. Among the sections altered in this edition are those on calcium metabolism and its relation to bone disease, the prenatal muscular dystrophies, intracranial suppuration, chronic mastitis, and endocrine disease. The lists of references at the end of each chapter have also been amended; these deserve praise for the judgment used in the selection only of key articles for insertion. It is perhaps unfair to criticise the book for omitting certain elementary sections. The authors specifically state that the text-book is intended for graduates and senior students with a certain knowledge of pathology; but even so the omission of discussions of general pathological principles, such as inflammation, leaves the vast store of information provided a little out of focus. The text is clearly written and easy to follow. The section on senile gangrene is misleading where it suggests that medical calcification, not atheroma, causes narrowing of the lumen in peripheral arteries. The illustrations are numerous and with two exceptions (Figs. 101 and 136) they are good. On the whole the book fulfils its purpose well and should prove of continued value to surgeons and advanced students of pathology.

Sanitary Inspector's Handbook

Second edition. By HENRY H. CLAY, F.R.San.I., F.I.S.E., Lecturer in Sanitary Engineering, London School of Hygiene and Tropical Medicine. With an introduction by Prof. W. W. JAMESON. London: H. K. Lewis and Co., Ltd. 1936. Pp. 432. 15*s*.

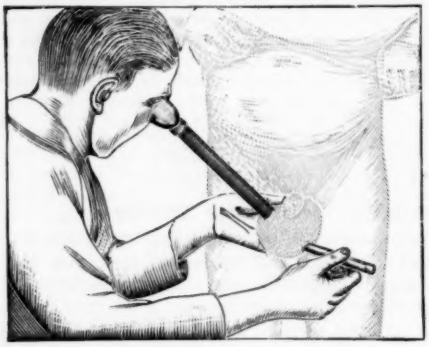
THE duties of a sanitary inspector are now so varied that any text-book attempting to cover them would be so long that its intention to instruct might be defeated. Mr. Clay's first problem must thus have been one of selection, and he has been successful in giving a well-balanced presentation of essentials. An obvious criticism is that urban conditions are given pride of place. For example, in the chapter on housing law and house inspection much space is devoted to overcrowding, which is the least important matter from a sanitary inspector's point of view, and little space to unfit and defective houses and the legal questions which may be involved in dealing with them. The structures of cowsheds and their inspection get small attention and the question of land treatment of sewage, a very practical one in rural areas, does not seem to be mentioned. It is not made clear that the methods described under house disinfection are applicable to tuberculosis, and the information in the section on graded milk requires revision. These points are noted and might well receive the attention of the author in a future edition. They do not detract from the practical value of the book, for we have here a clear and fairly put account of the various legal powers under which the sanitary inspector has to act, with practical hints how his duties should be performed. The work is clearly that of an able teacher and the book can be recommended not only to the student but to the experienced sanitary inspector.

NEW INVENTIONS

A POCKET TRANSILLUMINOSCOPE

ANYONE who is in close touch with clinical surgery will have seen scores of cases where the diagnosis has been vitiated, occasionally with disastrous

results, by not carrying out the test for translucency, or by carrying it out inefficiently. In the absence of a dark room a wooden stethoscope or a cardboard carton are helpful, but the former's calibre is too



small to make it reliable. The transilluminoscope here illustrated can be obtained from the Genito-Urinary Manufacturing Company at a very small cost. The rubber end-piece fits the eye accurately, and it renders eliciting the test for translucency a pleasure instead of a nuisance.

HAMILTON BAILEY, F.R.C.S. Eng.

THE LANCET

LONDON: SATURDAY, APRIL 18, 1936

TREATMENT WITH ACETYLCHOLINE AND ITS DERIVATIVES

THE work of DALE and his collaborators has made it clear that a large number of physiological actions are brought about by the liberation of acetylcholine, or some similar substance, at nerve-endings. This view has already shed light on such clinical problems as the action of Prostigmin in myasthenia gravis.[1] It is natural that interest should also have been aroused in the therapeutic possibilities of such a simple and powerful substance and in the last decade a large number of papers have been published claiming success from acetylcholine administration, mainly in vascular and gastro-intestinal conditions. So much information about pharmacological actions of acetylcholine is now available that a reassessment of its value in clinical medicine may be attempted. It is not a hormone in the sense that adrenaline is a hormone; it is not manufactured in a ductless gland nor carried in the blood stream to distant tissues, but is liberated at nerve-endings when the appropriate nerve is stimulated, after which it is rapidly destroyed by an esterase universally distributed throughout the blood and tissues. The labile nature of the compound would seem to render it at the same time an ideal chemical transmitter for physiological purposes and a substance with doubtful therapeutic applications. Carefully controlled studies on human subjects have, in fact, thrown doubt on its activity as usually administered. ELLIS and WEISS,[2] who studied the effects of continuous intravenous infusion, found that doses of 90 to 140 mg. a minute gave flushing of the skin, sweating, palpitation, salivation, nausea, and vomiting. The minimal effective rate of injection was found to be from 20 to 60 mg. a minute—which gives a rough measure of the rate of destruction of acetylcholine by the tissues—and the conclusion reached was that it is not a suitable therapeutic agent in diseases of the arterial system. CARMICHAEL and FRASER[3] have also examined the effect of intravenous doses of acetylcholine and report that single doses of 10 to 30 mg. gave the above-described subjective symptoms, slowed the heart for a few seconds, and lowered blood pressure. The effects passed off completely in less than a minute; they were abolished by atropine and accentuated if eserine had been previously given. CARMICHAEL and FRASER emphasise the great variability in the response of different individuals. Doses up to 500 mg. given subcutaneously or intramuscularly produced no subjective sensations and had no effect on pulse-rate or blood pressure even after eserine had been administered. Presumably therefore such results as have been obtained when acetylcholine has been injected therapeutically into subcutaneous tissues or muscle must be attributed to the small and variable amounts leaking into the blood stream from the very large doses injected. The greater part is probably inactivated at the site of injection.

The defects of acetylcholine as a remedial drug have stimulated the search for substances which would produce similar but more prolonged effects. Two of these have been fully investigated—namely, acetyl-β-methyl choline (Mecholyl) and carbaminoylcholine (Doryl). The former has an action like that of acetylcholine, but is less rapidly destroyed; it is more effective after subcutaneous injection and is active when given orally. In normal human beings it is about ten times as powerful as acetylcholine when given subcutaneously and much more constant in its action. The effects last for at least twenty minutes. ABBOTT[4] has shown that when given by mouth in doses of 300 mg. it relieves abdominal distension by causing contraction of the gut and increases the secretion of hydrochloric acid in achlorhydria. Of greater interest are the results obtained in cases of cardiovascular disease[5]; when given intramuscularly to patients with hypertension it produces a profound fall in blood pressure and may in some cases relieve headache, and in Raynaud's disease the symptoms may be relieved by its regular administration. In the treatment of paroxysmal tachycardia acetyl-β-methyl choline appears to be of great promise. Even allowing for the notorious difficulty in assessing the value of a remedy in this disorder the results recently reported by STARR[6] are striking; for on 66 of the 75 occasions on which it was given the paroxysms were promptly terminated—though in some of the cases it was necessary to press on the carotid sinus while the drug was acting. The dose required was less in young than in old patients, but a dose of 10 mg. seems to be safe in any patient over 20 years of age. The second derivative, carbaminoylcholine, was fully investigated pharmacologically in 1932 by H. KREITMAIR and by H. NÖLL, but seems to have attracted less attention from clinicians. Its actions are identical with those of acetylcholine but it is heat-stable, can be absorbed from the alimentary canal, and is less readily destroyed by the tissues. DAUTREBANDE and MARECHAL[7] have shown that doses of only 0·2 to 0·3 mg. intramuscularly give a definite fall of blood pressure which lasts for about half an hour, and this preparation appears preferable to acetyl-β-methyl choline where it is desired to give a drug of this type by mouth. Good results have been reported from the treatment of ozæna with a 0·05 per cent. aqueous solution of carbaminoylcholine for local application.

[1] THE LANCET, Feb. 29th, 1936, p. 491.
[2] Ellis, L. P., and Weiss, S.: Jour. of Pharmacol., 1932, xliv., 235.
[3] Carmichael, E. A., and Fraser, F. R.: Heart, 1933, xvi., 263
[4] Abbott, W. O.: Amer. Jour. Med. Sci., 1933, clxxxvi., 323.
[5] Starr, I., Jr.: Ibid., 1933, clxxxvi., 330.
[6] Starr: Ibid., February, 1936, p. 210.
[7] Dautrebande, L., and Maréchal, R.: Compt. rend. Soc. de biol., 1933, cxiii., 79.

A word of warning is necessary about the toxic effects which may arise during treatment with these drugs. The desired effects on the heart or vessels can rarely be brought about without some undesirable side-effects such as sweating, salivation, or (more rarely) nausea, and it is advisable to prepare the patient for such symptoms. The drugs should always be given with the patient lying down to avoid syncopal attacks, which may be brought about by the fall in blood pressure. It is wise to avoid giving them in cases of angina pectoris, since substernal pain has occurred after their use, and PAGE [8] has shown that acetyl-β-methyl choline may temporarily invert the T wave in all leads of the human electrocardiogram. Their employment is also contra-indicated in patients with gastric hyperacidity. The really dangerous effects may occur in two ways. A dose of acetylcholine or its derivatives intended for subcutaneous use may be given by mistake intravenously; in this way 30 mg. of acetyl-β-methyl choline has caused cardiac asystole for seventy seconds. Equally serious is the risk that one of the highly active derivatives of acetylcholine may be given subcutaneously in doses which would be reasonable for the unstable parent substance.[9] It is advised therefore that a syringe containing a full dose of atropine be kept at hand ready for intravenous administration whenever one of this series of drugs is being injected.

It seems that these derivatives of acetylcholine have a definite but restricted place in therapeutics; and it might be advantageous if they came to replace acetylcholine itself, which is always inconstant in its effects and often entirely inactive.

CONTINUOUS VENTRICULAR DRAINAGE IN CEREBRO-SPINAL FEVER

Dr. HAMPSON points out [10] that, of all forms of meningitis in infants, that caused by the meningococcus offers the best chance for effective treatment—provided it can be recognised in good time. In milder cases especially, the early appearances may be deceptive, the condition being diagnosed, without lumbar puncture, as meningism. Diagnostic puncture, with removal of 1·0 c.cm. of fluid for examination, is quite harmless, and in HAMPSON's opinion its more frequent performance would avert many tragedies. It is in the less serious cases which have been missed, and those in which treatment has been only partly effective, that the late sequel of posterior basic meningitis (recognised by G. F. STILL in 1898 as a meningococcal infection) is to be apprehended. The clinical picture, which appears to be associated with thick purulent exudate at the base of the brain, is graphically described by HAMPSON but may here be summarised in the term opisthotonos. Partial occlusion of the foramen of Majendie, and excessive production of cerebro-spinal fluid, lead at length to a condition of internal hydrocephalus which if unrelieved results in death, or, at best, mental defect.

If meningitis is recognised very early, intravenous injection of antimeningococcal serum may bring about rapid improvement, and HAMPSON advises the use of a mixture of the available commercial sera without waiting for laboratory findings. Because of the risk of adhesions from an "aseptic meningitis" he hesitates to employ the intrathecal route before the organism has been typed and a serum provided which agglutinates it; but the intramuscular route is unobjectionable. In the series recorded in his paper an autogenous vaccine, the initial dose of which, for fear of troublesome reactions, was not allowed to exceed half a million organisms, gave promising results in two or three cases. Daily lumbar puncture, supplemented by cisternal puncture if the lumbar tap is dry, and the introduction through the needle of a suitable serum, should be maintained until cultures of the fluid, which should be almost clear, are constantly negative; thereafter the intervals of treatment should be lengthened. Sometimes, possibly owing to the provision of complement, a single blood transfusion is dramatically successful. When complete block had occurred and all methods of withdrawal of fluid had failed, continuous ventricular drainage proved successful in 24 out of 25 cases in overcoming the block and re-establishing normal flow. Many of the children so treated were moribund; even so, 6 recovered and HAMPSON believes that earlier resort to ventricular drainage would have saved more lives. The avoidance of daily puncture, which the child comes to dread, and the relief from an irksome posture and from vomiting, make the procedure well worth while even in the apparently hopeless case.

A small opening is made in the skull over the posterior horn of the lateral ventricle; to effect this in older children a burr is required, but in infants a trocar suffices. The cannula to be inserted is mounted on a hollow trocar through which runs a hollow guide and through this again a blunt-pointed stilette, its lower end grooved and its upper end cone-shaped. The cone permits and controls the escape of fluid. The guide is pushed into the ventricle; the depth of insertion is noted and cautiously increased until the medial wall of the ventricle is touched. The depth is again noted and the guide withdrawn to the mid-point of the two readings; a sufficient depth of insertion is important. Trocar and cannula are then pushed along the guide to the same depth, usually about 3·5 cm. Slight withdrawal of the stilette permits of a slow escape of fluid and obviates a sudden fall in ventricular pressure when the trocar guide and stilette are next withdrawn and replaced by a two-way inner cannula provided with a small lateral tube for irrigation. The larger tube of the inner cannula is connected to a collecting-bottle the height of which can be adjusted to control the pressure in the ventricle. The outer cannula is kept in position by a clamp fitted with a ball-and-socket joint and a webbing strap. For the first 24 hours the joint is unclamped; contraction of the ventricle, resulting in the tube being carried forward, might injure the brain. Unless the pus is very thick, artificial irrigation is not

[8] Page, I. H.: Amer. Jour. Med. Sci., 1935, clxxxix., 155.
[9] THE LANCET, Feb. 15th, 1936, p. 391.
[10] Hampson, A. C.: Guy's Hosp. Rep., 1935, lxxxv., 431.

called for; the cerebro-spinal fluid itself irrigates sufficiently. Serum may be introduced through the apparatus. Usually after two or three days fluid can be withdrawn by cisternal puncture, and thereafter saline and serum can be run through from ventricle to cistern. Ultimately, when the character of the fluid is satisfactory, the cannula is gradually and cautiously withdrawn, and finally the wound is closed with a collodion dressing. Dr. HAMPSON emphasises the paramount importance of expert nursing in securing changes of posture, cleanliness, and nutrition. Most of the breast-fed babies were kept on the breast—a tribute, he adds, to the nursing staff and, not least, to the mother.

THE ADELPHI

THE demolition of the central block of the Adelphi buildings, which has for its front the famous terrace overlooking the Thames, is due to start at any moment, and the circumstances which have led up to the widely criticised action illustrate in a striking way situations that must become increasingly frequent in large cities. The claims of the old for preservation, made strong by history or sentiment, must yield to the claims of the new which arise out of the needs of developing society. That in a general way will be accepted, but acquiescence does not imply any universal endorsement of the value or virtue of the building developments now going on in the older districts of the metropolis; and the questions that are arising in London with growing frequency confront all who dwell in old and important urban communities. Two things, it would seem, should be made clear in connexion with these operations of destruction and substitution—first, that the old buildings have outgrown utility, and, secondly, that the structures which rise in their place meet real needs and have not as their justification only the making of money, whether on behalf of rating authorities or of personal speculators. The great justification of rebuilding schemes is that they promote health in the widest sense, not only by modern sanitation and amenities, but also by providing facilities for the discharge of necessary work. If these two things can be proved history and sentiment must be ignored, however regretfully. Regarded in this way no valid arguments can be advanced against the demolition of the Adelphi. The charming structures have outlived their practical utility, and in face of this fact the plea for the preservation of the picturesque cannot prevail.

The cultured and leisured sections of the population, for whom ROBERT ADAM and his brothers designed the Adelphi quarter, have left it long ago; their followers, men of literary and artistic proclivities, who gave the Adelphi throughout the nineteenth century its fascinating and slightly humorous distinction, have gradually ceased to occupy the lovely rooms, one well-known social club remaining till the end as the sole representative of this aspect. The slow desertion of the Adelphi by artists, in words or materials, by critics and journalists and their friends and imitators, proves that the buildings no longer conform sufficiently to modern standards of life, and those who once competed for the semi-cloistered shelter afforded in an elegant example of town-planning have found in other places their more convenient if less happily situated abodes. There is therefore no widespread grievance following on dispossession, such as must be grievously felt in many quarters of London to-day, where small houses, charming in character, standing in their own greenery, and conforming entirely to the needs of their tenants, are being torn down to make place for masses of flats, generally described as offering luxury while constituting a curious commentary on what luxury means.

No medical conveniences or facilities happen to be lost by the disappearance of the Adelphi central quadrangle, and the present home of THE LANCET, with its fascinating view along the main artery of John-street, remains undisturbed. Moreover the Adelphi at no time housed more than an occasional doctor, though medical practitioners some hundred years ago found in the neighbouring streets on both sides of the Strand favourable opportunities for practice. But one doctor who lived on Adelphi-terrace made it famous in the painting world. This was THOMAS MONRO, member of a distinguished medical and artistic family. His grandfather, his father, and his uncle all made their mark in medicine, but two at least were men of high culture as well as distinguished physicians. THOMAS MONRO, himself an accomplished doctor, a leading authority on lunacy, and physician to George III. moved from Bedford-square to 8, Adelphi-terrace in 1793. He was a considerable artist and had inherited through his father or personally collected many pictures and drawings by famous eighteenth century painters, notably by GAINSBOROUGH and J. R. COZENS. The great English school of water-colour painters had its practical origin in 8, Adelphi-terrace, where THOMAS MONRO assembled a group of young artists in evening classes, lent his paintings and drawings to be copied, and stimulated in every way any promising achievement. He was astonishingly fortunate in his recruits, for among those who profited by his enthusiasm and generosity were TURNER, GIRTIN, VARLEY, PETER DE WINT, and JOHN LINNELL. How the work of these men and their followers became the starting-point of the peculiarly English achievement of water-colour painting is a well-known and interesting feature in the history of art, and the names of the Adelphi and Dr. THOMAS MONRO are thus assured of preservation.

THE Government of South Australia is collaborating with the University of Adelaide in establishing an institute of medical science. The sum of £15,000 has been privately subscribed for the purpose, and the Government will make an equal contribution. As announced on p. 927, Dr. E. Weston Hurst, of the Lister Institute, London, has been appointed the first director.

ANNOTATIONS

DISEASE AND WORK

AT the Cambridge meeting of the Tuberculosis Association, of which some account was given in our last issue, Freiherr V. von Weizsäcker, director of the medical clinic at Heidelberg, had some provocative things to say about disease and work. At present, he remarked, we were wasting time and money in endeavouring to restore a function, instead of spending time and money in adapting the diminished or altered function to existing conditions of employment. A patient treated by a merely reparative therapy—no matter whether the primary disease was tuberculosis, concussion, ulcer, or sciatica—is apt to develop what is known in Germany as "secondary symptoms," caused by a rupture of life's coördination in work, wage-earning, respectability, and physical enjoyment. This "interruption factor" in recovery is usually reinforced by a number of typical conflicts of a more or less social nature, such as unemployment with its attendant poverty, disputes with a superior, family quarrels, political antagonism, or litigation, in which the patient is contesting only for his rights as such, and not for definite material advantage. Prof. Weizsäcker has in his own practice as internist and neurologist discovered the significance of these and similar factors in the treatment, not only of neurosis and incapacity for work, but even of purely "organic" disease. The definition of work is only to limited extent a question of physiological economy; even in the case of certain forms of manual labour the quality of the work—e.g., its exactitude or beauty—is of greater importance than the output of physical energy required in its performance. Capacity for work is not a question of physiological economy, but of will-power; of conditioned will, that is, not of conditioned reflexes. This being so, Prof. Weizsäcker does not find it surprising that neither the economic quotient, nor the basal metabolism, nor the absorption of oxygen shows characteristic alterations in the case of the tuberculous patient with impaired working capacity. More is to be expected from a searching social analysis than from a blood count. But then the Heidelberg professor does not regard work as a religion; in certain cases it may be better, he dares to suggest, to learn to use leisure—e.g., in reading, talking, observing, learning to think. His paper produced a remarkable impression. In the discussion which followed Dr. W. C. Fowler drew attention to the metabolic value of work, and deprecated the idea—so prevalent among patients, and even held by some doctors—that breakdown is always associated with work. It was much more often, he thought, associated with recreation. Dr. F. R. G. Heaf thought the sanatorium patient should be asked if he *liked* to do work; once his will was enlisted there was much less chance of any trouble over it. The educational side of work should be stressed.

CHANGING ANÆSTHETICS

SOME years ago Mr. Bernard Shaw's gibe against medical men that their anæsthetics "spare us nothing except the actual pain of operation" must have gone home. That day is fortunately past, and the patient who has to undergo an operation nowadays, whatever else he fears, need not fear the suffocation which used to precede anæsthesia or the prolonged discomfort which followed it. This improved state of affairs is due largely to the work of the chemists and pharmacologists who have supplied the anæsthetist with effective drugs for easing the road into unconsciousness. These drugs have done more. When they have not abolished altogether the need for chloroform and ether, the two anæsthetics mostly responsible for after-effects, they have reduced the amount that has to be administered. The use and character of the various adjuvants at the anæsthetist's disposal are well set out in a recent paper[1] by Dr. Frankis Evans, anæsthetist to St. Bartholomew's Hospital. Although he applauds the methods which he describes, Dr. Evans does not fail to pay tribute to the results achieved by the older anæsthetists with their limited means, inviting us to marvel with due humility at the wizards who wielded drop-bottle and square of lint. In one respect the anæsthetist of to-day does not yet appear to have surpassed his forerunners. The patient's comfort and the surgeon's facility have both been enormously enhanced; we doubt whether it can be maintained that the patient's safety has been increased to the same extent. The anæsthetist must not be content to rest on his laurels so long as ether convulsions, "status lymphaticus," post-operative shock, and post-operative pneumonia continue to claim their victims.

BIOLOGICAL PRINCIPLES IN ORTHOPÆDIC SURGERY

IF the skeleton is regarded as still in process of evolution, with an imperfect adaptation to the erect posture and a partial obsolescence of certain of its structures, many problems of orthopædic surgery will become simpler. This is the main thesis of a paper[2] by Dr. George W. Hawley of Connecticut. He enunciates the general principle that "involuting structures are potentially weak and vulnerable, those in the process of evolution are particularly strong and resistant to disease and injury." It is doubtful, however, whether this statement can be accepted in its present form. When he cites the shoulder-girdle as a structure that has largely lost its function and power in supporting and moving the body-weight—as in climbing trees—it is easy to follow him: undoubtedly the clavicle and the shoulder-joint are particularly liable to injury when the arm is held out of the pendent position. But the vulnerability of his "principle" is apparent when he describes the foot as also weak because in process of "involution." The human foot is surely a highly differentiated structure, adapted for support and for the distinctly human function of walking. Hawley believes that the foot would be structurally and functionally stronger if all the bones below the astragalus were ankylosed. But that is to presuppose that dancing is not one of its functions. Nevertheless, it is probably right, in *operations* on the foot, to aim at an ankylosis, because in most feet the muscular and ligamentous elements are poor and will not be much help in rendering a foot both mobile and strong. The liability of the spine to sprains and injuries of all degrees of severity can also be related to its imperfect balance and adaptation to upright posture: spondylitis may be due to instability of the curves of the spine and the irregular strain to which they are subjected. The biological "law" is instability of form with instability of

[1] St. Bart.'s Hosp. Jour., March, 1936, p. 106.
[2] Amer. Jour. Surg., March, 1936, p. 438.

function; structures are weak which are in process of changing their form and function.

The effect of an individual injury to the skeleton is largely determined by the age of the bones and ligaments involved, and deformities are not likely to be corrected spontaneously in later life. It is a curious fact, however, that activity of bone repair differs very little at different ages. At all ages it is preceded by a retrogression to a primitive type of connective tissue, and this tissue may be in some sense "young" again. The healing of ligaments and of muscles, on the other hand, seems to be a much more perfect process in the young than in the middle aged or old. Who ever saw a child with a stiff knee after a fracture of the femur?

SENSE OF SMELL

DURING the past year Dr. C. A. Elsberg of New York and his colleagues have been carrying out important researches on the physiology of smell.[1] Their objective is to devise methods which can be applied in clinical practice for diagnostic purposes in much the same way as are the refined tests for vision and hearing. There is no doubt that the sense of smell has been neglected in favour of the other two special senses, and that a suitable test might give a great deal of information, unobtainable by other methods, with regard to lesions within the cranial cavity. The idea is not new, but most of the previous tests used have been dependent on the patient's sniffing up some odorous substance, and are accordingly not clearly objective. Elsberg's method requires no coöperation on the part of the patient beyond a description of his sensations, which cannot very well be eliminated. A fixed quantity of odorous substance is placed in a bottle of known capacity so that the volume of air above the liquid is always constant. The stopper carries two tubes, one of which communicates with the patient's nostrils through an ordinary double nose-piece, while through the other tube a measured amount of air can be injected into the bottle by means of a syringe. In carrying out the actual test the nasal tube is occluded, a few cubic centimetres of air are introduced into the bottle, the pressure inside the bottle thus being raised. The patient is instructed to hold his breath and the clip on the nasal tube is opened. The result is that a puff of air is blown into the patient's nostrils, the volume and pressure of which depend on the amount of air previously injected into the bottle. With small quantities of air the subject smells nothing, but as the volume of successive injections is gradually increased he becomes able to detect the presence of an odour. He then recognises that the odour is familiar, and finally is able to identify it. (This recalls the stages in the visual perception of colour.) The least injection which leads to the identification of an odour is known as the olfactory coefficient of that odour, and this is expressed in cubic centimetres. If only one nostril is used for the test, the other being occluded, the quantity is known as the minimum identifiable odour (M.I.O.).

Preliminary tests on normal persons have revealed certain interesting facts, not the least important of which is that under standard conditions the olfactory coefficients of numerous substances are almost the same from individual to individual. Another interesting observation is that the olfactory coefficients vary as the boiling-point of the substance used, and are therefore presumably dependent on its vapour pressure. This relationship is so constant that if the boiling-points of two substances are known, together with the olfactory coefficient of one of them, the olfactory coefficient of the other can be predicted with accuracy. The authors point out that very little is known about the properties on which odour depends, but the simplest explanation of these findings is that the amount of a substance which will dissolve in the film of liquid covering the olfactory nerve-endings depends on its partial pressure. This should also depend on a further factor—namely, the force of the "blast injection" and the degree to which this momentarily raises the pressure in the nose. This has been confirmed experimentally.

A second test is known as the "stream injection" test, whose title is self-explanatory. By this method it can be ascertained whether the substance under investigation stimulates the endings of the trigeminal nerve, and it is found that very few odorous substances which are likely to be recognised by a patient are free from a "trigeminal component." For clinical tests the actual perception of odour by each nostril, the fatiguability of the olfactory sense, and the reaction to trigeminal component if this exists are determined. Although relatively few conditions have so far been investigated, it is found (1) that a neoplasm pressing on an olfactory nerve or tract increases the M.I.O. of that side; (2) in intracerebral tumours the M.I.O. remains normal but olfactory fatigue lasts longer on the side of the neoplasm—in a generalised increase of intracranial pressure the M.I.O. may be lower than normal; (3) intracerebral tumours which also press on the olfactory bulb (e.g., frontal lobe tumours) lead both to an increase of M.I.O. and a longer duration of fatigue.

This technique promises to be of clinical value. The apparatus is simple, the reagents suggested are few (namely, coffee, citral, benzaldehyde, and oil of turpentine), the procedure is harmless, and there seems no reason why it should not be widely tested.

OSTEOPOROSIS OF ENDOCRINE ORIGIN

A CASE of localised rarefaction of bone leading to fracture and relieved by administration of ovarian extract is reported by Baumgartner and Berthoud.[1] The patient, a woman of 33, had had both tubes, one ovary, and the greater part of the other removed eight years previously for a bilateral salpingo-oöphoritis. When first seen she complained of a painful swelling of the right knee, for which she had undergone manipulative treatment without relief. A radiogram showed osteoporosis of the upper end of the right tibia and fibula. Rest and cold compresses relieved the pain, but six months later the upper epiphyses of the tibia and fibula were fractured by a trivial fall. The fractures were reduced and the leg put up in plaster. Because the patient showed signs of ovarian deficiency—almost complete amenorrhœa and hot flushes—it was thought that the osteoporosis might be due to an endocrine imbalance, and she was treated for three months with injections of an ovarian preparation. At the end of this time it was found that new trabeculæ had been laid down and the bony structure resumed its normal radiographic appearance. According to Leriche and Policard osteoporosis follows local hyperæmia; and the fact that deficiency of ovarian secretion may cause vasomotor disturbances is obvious from the hot flushes so often seen at the menopause. In the

[1] Bull. Neurol. Inst., New York, 1935, iv., 1, 5, 20, 26, 31, 264, 270, 286, 479, 498, 501, 511.

[1] Baumgartner, J., and Berthoud, F.: Presse méd., 1936, xxiv., 495.

interesting syndrome accompanying basophil adenoma of the pituitary (Cushing's syndrome) localised rarefaction of bone is frequently found and may give rise to kyphosis or to spontaneous fractures of long bones. This condition is usually associated with loss of function of the sex glands—with amenorrhœa in the female and impotence in the male. Osteoporosis associated with ovarian deficiency does not appear to be due to generalised disturbance of calcium metabolism, for the serum-calcium level both in Cushing's syndrome and in the other cases recorded is within normal limits. It seems to be attributable rather to a vasomotor disturbance, leading to localised hyperæmia, than to disturbance of parathyroid secretion.

TREATMENT WITH LARGE DOSES OF ATROPINE

INTEREST in the action of large doses of atropine in man has been aroused again by the Kleeman[1] method of treating cases of post-encephalitic parkinsonism. Bremer's[2] observations, out of which this form of treatment arose, seemed to indicate that parkinsonians have an unusual degree of tolerance to this drug. D. Danielopolu and N. Radulesco in Bucharest have re-examined the problem of tolerance to atropine in man, and have applied the method of high dosage to conditions other than the post-encephalitic syndrome. Their observations were communicated at the first meeting of a new body, the Rumanian Academy of Medicine, and are recorded in a series of articles in the first issue of its journal, the *Bulletin de l'Académie de Médecine de Roumanie*. Prof. Danielopolu is the secretary-general of the Academy, which has two divisions: one is devoted to the medical and biochemical sciences and the other is concerned with medical organisation, public health, and conditions of practice.

Danielopolu and Radulesco do not consider that post-encephalitics are especially tolerant to atropine, since they were able to show that tolerance can be developed by most people if the drug is given in gradually increasing doses. Patients with pyloric ulcer were studied and were given at first injections of a milligramme (1/64 grain) of atropine a day in divided doses; the dose was raised by a milligramme a day until as much as 19 mg. a day in one case, or (averaging the dose in eight cases) 10 mg. a day was being taken. Such doses brought about surprisingly little alteration in heart-rate, blood pressure, or gastric acidity. It is believed that atropine given in this way diminishes the tone of the whole autonomic nervous system, sympathetic as well as parasympathetic, and it is proposed to apply the results to the treatment of a number of disorders such as asthma and thyrotoxicosis. Sea-sickness has already been treated successfully by this method. For short crossings it is sufficient to take 0·5 mg. (gr. 1/120) of atropine sulphate about an hour before embarking. Before long voyages, however, subjects susceptible to sea-sickness are given atropine as follows. Four days before embarking, 1 mg. is given in four doses; the dose is increased by a milligramme a day so that 4 mg. is taken during the day of departure, and this dose is maintained throughout the voyage. The dosage must be reduced gradually after the voyage ends. The administration of atropine in exactly the same way is advised before operations in which chloroform is used, for it is believed that fatalities during anæsthesia may thus be avoided, and nausea and vomiting during recovery eliminated. If respiration stops in patients who have been prepared in this manner, pressure on the carotid sinus causes breathing to recommence without affecting the heart.

These authors remark on the dangers attached to the sale of mixtures of morphine and atropine. A morphinomaniac may mistake a mixture of morphia and atropine for pure morphia and thus receive a toxic dose of atropine. The morphia habit, moreover, is especially easily acquired by those who use a mixture of atropine and morphine, since they become tolerant to the unpleasant effects of atropine, while the atropine continues to relieve many of the unpleasant actions of morphine.

[1] Kleeman, A.: Deut. Zeits. f. Nervenheilk., 1929, cxi., 299.
[2] Bremer, F. W.: Deut. Arch. f. klin. Med., 1925, cxlix., 340.

THE YOUNG DOCTOR IN AMERICA

Mr. G. H. Edington, addressing the students of St. Mungo's College, Glasgow, last month, is reported to have expressed the view that nowadays "there is far too much talk of remuneration" for work done by doctors. Do the recently qualified men in this and other countries agree with him, or are they inclined to regard as cant the suggestion that their professional aims are less mundane than those of their fellow-men? Certainly those practising in some European countries at the moment would not agree that the question of remuneration could safely be neglected. That is not to say that it should obsess the student, or be the motive power in his choice of a profession. Dr. Nathan B. van Etten has attempted[1] to discover whether young persons in the United States of America take up the study of medicine from a desire for social service or from a taste for pure science, or whether they seek merely social distinction or material gain. He comments, doubtless authoritatively, on the high code of ethic maintained by the bulk of the profession during the past 2000 years. Of the 150,000 doctors in the United States, two-thirds belong to the American Medical Association and, in increasing numbers, are joining county medical societies "prompted by a desire for group protection, by a desire to follow the currents of scientific thought and by a growing appreciation of the importance of political organization." The United States medical service, he holds, perhaps naturally, to be the best in the world. In that country institutional treatment is replacing home treatment; municipal hospitals are superseding voluntary hospitals. The time is coming, he thinks, when every citizen will be entitled to treatment in a municipal hospital and when the staffs of these hospitals will be paid for their work. These changes, if they come, will profoundly affect the private practice of the future. Nevertheless more and more young persons wish to practise medicine. The proportion of patients to doctors is already less than 800 to 1 and still twice as many doctors are licensed annually as die. Dr. van Etten thinks that too often the young doctor is ignorant of economics and the practicalities of medical problems. So abstract is his education that it leaves him no opportunity for the proper study of mankind. For this he blames the academic detachment of the teacher who "does not care for general contacts" and "fails to function as a citizen." Dr. van Etten would have the teacher prepared to teach practical economics and to be "a good mixer" at any rate with his medical colleagues in private practice. At the December examination, 190 candidates from 42 medical schools applied for 16 internships at the Morrisania City

[1] Jour. Amer. Med. Assoc., March 7th, 1936, p. 772.

Hospital. Many of these candidates had achieved considerable academic success at their various medical schools. They were asked questions of a severely practical nature and only five of them were found suitable for appointments. In answering the questions most of them concentrated on inessentials. Dr. van Etten concludes that the young doctor's social objective may not point higher than making an honest living, but if this aspiration is based on respect for a high quality of service the health of our people will be in safe hands. To achieve it, teachers must become active members of medical organisations, select fewer students, teach clinical medicine intensively, promote "inspirational preceptional contacts" (whatever that may mean) between themselves and their pupils, and finally try to develop a spirit of civic responsibility. With all respect to Dr. van Etten's views, we question whether the problem is really so serious. Assuming, fairly or unfairly, that the American medical student may lack the same measure of liberal education and intensive clinical teaching as obtains in this country, we doubt very much whether, once established in private practice, he will long remain ignorant either of practical economics or of his fellow-men.

THE PHLYCTEN

THE phlycten, it seems, is not a specific localised reaction of the conjunctiva; it occurs also in acne rosacea, Koch-Weeks conjunctivitis, and a number of other conditions besides phlyctenular ophthalmia. The pseudophlyctens observed in tropical countries and the adult preponderance in the incidence of phlyctenosis in Japan are other points in favour of the multiple ætiology of the phlycten, which was the theme of a paper contributed by Mr. Arnold Sorsby, Dr. R. Hamburger, and Dr. L. R. Benham to the congress held this month in London.[1] Since 1887 Burchardt has claimed that inoculation of staphylococci can produce phlyctens. More recent work however makes it unlikely that extraneous factors are responsible; a mass of experimental evidence supports the view that the phlycten is an anaphylactic response of the conjunctiva in a sensitised subject. This sensitisation may be tuberculous or produced by a wide range of substances such as tyramine, calcium caseinate, horse serum, and cocaine. A positive tuberculin reaction is common in phlyctenular ophthalmia; among 4000 cases collected from the literature the proportion was generally between 80 and 90 per cent. A higher incidence was noted among 688 cases under the age of 6 years analysed by the authors, and in these the suggestion of tuberculous infection was re-enforced by detailed radiological study of the chest. Among 130 phlyctenular lesions under the care of Mr. Sorsby and his colleagues at White Oak Hospital, Swanley, 75 per cent. were Mantoux positive, against 20 per cent. in a control series of 122 blepharitis cases. If only cases under 6 years old were considered the corresponding percentages were 70 and 9·4. In 116 cases of phlyctenular keratitis and 87 control cases of blepharitis examined radiologically, tuberculous lesions of the chest were shown to be present in 71 and 16 per cent. respectively (with suspected activity in 20 and 3 per cent. respectively); distinctly negative X ray findings were obtained in 13 and 58 per cent. respectively. Clinical tuberculosis was however present to a much smaller extent, there being only 3 cases in the phlyctenular group, The results of stomach washings were completely negative for a series of 50 phlyctenular cases and a control group of 8 blepharitis cases. The evidence for a tuberculous factor in phlyctenular ophthalmia was strengthened by the finding of 14 cases of active tuberculosis subsequently admitted to L.C.C. hospitals out of a series of 238 phlyctenular cases admitted to Swanley from 1924 to 1930, making a percentage of 5·9, or approximately ten times the notification rate for children of the corresponding ages. Mr. Sorsby concluded by drawing a distinction between tuberculous infection and tuberculous disease. In the great majority of cases phlyctens are to be regarded as a manifestation of tuberculous infection at an early age; phlyctenular cases, like the majority of infected children, generally overcome the infection. A larger proportion of the phlyctenular cases than of the normal child population do however fall victims to tuberculosis, probably because of their early infection. In the discussion that followed Mr. R. E. Bickerton supported Mr. Sorsby's contentions. The importance of tonsillar sepsis as an ætiological factor was emphasised by Mr. C. B. Goulden, of intestinal toxæmia by Dr. A. J. Ballantyne.

[1] THE LANCET, April 11th, p. 842.

THE NEW ERGOT ALKALOID: A QUESTION OF NOMENCLATURE

THE Council on Pharmacy and Chemistry of the American Medical Association[1] announce the result of their consideration of the question of the proper name to be applied to the new ergot alkaloid, which has been described by Dudley and Moir as "ergometrine," and to which the names ergotocin,[2] ergobasin, and ergostetrine have been applied by other investigators, who obtained the substance at about the same time. A statement recently published in *Science* and in *Nature*,[3] and signed on behalf of the four laboratories concerned, had settled an outstanding question by stating definitely, on the basis of comparisons of samples carried out in all four laboratories, that the alkaloids to which the four different names had been given are one and the same. It was therefore only the question of choosing one suitable name, for general application to the one substance, on which the Council had to deliberate. "It is necessary," they state, "that a suitable, *non-proprietary* name *not therapeutically suggestive* be adopted for the new alkaloid. Not one of the several names that have been proposed by the discoverers complies with these requirements."

The name ergometrine was given to the alkaloid by Dudley and Moir, in their paper containing the first description of it, as a purely scientific name. Afterwards Dudley published a full description of the method of isolating this alkaloid from ergot, and obtaining it in pure condition. This method was published for the information of anybody who desired to undertake the practical preparation of the alkaloid; and there is no reason to suppose that any method differing from it in essential particulars has, in fact, been used for this purpose. There was therefore no question in this case of any attempt to obtain for anyone a proprietary interest in the alkaloid, by secrecy, or by protection either of the method of its preparation or of the name ergometrine proposed for it. It must, accordingly, be supposed that the members of the Council on Pharmacy and Chemistry regarded ergometrine as an unsuitable name for the alkaloid, not on the

[1] Jour. Amer. Med. Assoc., March 21st, 1936, p. 1008.
[2] Ergotocin and ergostetrine are known commercially in U.S.A. as ergotrate and ergoklinine respectively.
[3] Nature, March 7th, 1936, p. 403.

ground that it is a proprietary name, but on the alternative ground that it is "therapeutically suggestive." This seems to us far-fetched; it is certainly not as suggestive as the names of many more familiar alkaloids—morphine and narcotine for example. Knowledge of Greek is not so widespread that the ordinary reader will connect ergometrine with a stimulant action on the uterus; and if this is the difficulty it may be argued that the word ergot, embodied in the Council's new name "ergonovine," is equally obnoxious.

In issuing their list of New and Non-official Remedies for the guidance of the medical profession the Council do work of great value; and nothing but respect can be felt for their motives and general policy. But such a service does not, as they admit, give them a right to put aside the traditional prerogative of the discoverer to propose, for scientific use, a name for a substance which has been made or isolated as the result of his researches. The workers who in 1932 first demonstrated the existence of a hitherto unrecognised active principle in ergot, who in 1935 isolated and identified this principle as a new alkaloid, and who were the first to describe its chemistry and pharmacology in terms by which it could be clearly recognised and differentiated by other workers, named the substance ergometrine. We see no need to depart from this name. It seems a clear case for an international ruling.

PSYCHIATRIC IN-PATIENTS AT A GENERAL HOSPITAL

St. George's Hospital has issued the first number of a magazine called *Rebuilding*, in which the editor expresses the hope, which must be unique among editorial aspirations, that the number of issues published will be few. Three or four numbers are to appear every year until the new hospital is so well on its way that the need for such publicity comes to an end. The rebuilding of a great London hospital must interest a considerable number of people in addition to those actually associated with the institution, and we have no doubt that the energy with which the campaign to get the necessary money for St. George's is being pursued will accelerate to the point at which building operations can actually begin. The sketch plans are already made and under discussion; the number of complicated questions which have to be solved before a modern hospital can begin to arise, and the difficulties in reconciling the architectural requirements with those of the medical, surgical, and special departments make it desirable that as much time as possible shall be spent in considering them. An interesting innovation for a general hospital will be a psychiatric in-patient department—a clinic with some sixty beds to be divided between men, women, and children, which will be filled mainly from patients attending the out-patient psychiatric department. This seems to us a progressive step. Not only will it provide increased facilities for treating the many patients whose disability is really not so much physical as mental, but, almost more important, the student will be enabled to see, as at present he cannot in hospital practice, how large a part in determining the inefficiency of human beings is played by influences that cannot be classified under any of the recognised organic diseases. The young doctor beginning private practice is generally more puzzled than by any other experience by the fact that many of his patients are suffering from no definite complaint in the cure of which he has been trained. Many of these people are in the early stages of what may become definite neuroses or even psychoses. Others perhaps could be put into no definite category of nervous disease, but are none the less in need of expert help. A department such as that outlined for St. George's should do much to teach the future practitioner to give it to this large groups of patients.

Summer Time will commence in Great Britain, Ireland, the Channel Islands, and the Isle of Man on Sunday morning next, April 19th, at 2 A.M., when the hands of timepieces should be advanced one hour. It will end on Sunday, Oct. 4th.

WE regret to announce the death of Mr. John Gordon Harrower, professor of anatomy at the Medical College, and consulting surgeon to the General Hospital, Singapore, at the age of 46.

WE have also to record that Prof. Robert Bárány, of Vienna and Upsala, died on April 8th. Prof. Bárány, who was 59 years of age, was awarded the Nobel prize for his work on the physiology and pathology of the vestibule of the ear, and his name is applied to tests which he described. It will be recalled that only six weeks ago he contributed to our correspondence columns a letter advocating intranasal submucous injections of calcium in the treatment of excessive nasal secretion.

THE SERVICES

ROYAL NAVAL MEDICAL SERVICE

Surg. Lt.-Comdr. A. N. Forsyth and Surg. Lt. (D.) H. V. Pell to *Victory* for R.N.B.

ROYAL NAVAL VOLUNTEER RESERVE

Surg. Lt. W. H. Roberts promoted to Surg. Lt.-Comdr.

ROYAL ARMY MEDICAL CORPS

Lt. J. O'Connell to be Capt.

TERRITORIAL ARMY

Lt.-Col. R. I. Dacre, T.D., resigns his commn. and retains his rank, with permission to wear the prescribed uniform.

Capt. C. J. L. Wells relinquishes his commn. and is granted the hon. rank of Capt.

Capt. A. D. Rope resigns his commn. and retains his rank.

To be Lieuts.: 2nd Lt. W. B. R. Monteith (late R.G.A.), T. W. Preston (late Cadet Corpl., Alleyn's Sch. Contgt., Jun. Div., O.T.C.), and F. G. Maitland.

ROYAL AIR FORCE

Dental Branch: Flight Lt. A. Maben to R.A.F. Hospital, Aden. The undermentioned are granted non-permanent commissions as Flying Offrs. for three years on the Active List: O. F. Brown, I. St. C. Alderdice, J. H. G. Fensom, S. Hill, R. A. Pepper, and W. A. H. Smith.

INDIAN MEDICAL SERVICE

Capt. A. M. Fraser retires, receiving a gratuity.

The undermentioned officers have vacated appts. in India:—D.A.D.H.: Maj. J. W. F. Albuquerque. D.A.D.P.: Capt. M. K. Afridi.

The undermentioned appt. has been made in India:—D.A.D.P.: Maj. J. W. F. Albuquerque.

ROYAL NATIONAL OPHTHALMIC HOSPITAL, LONDON. Last year 3739 in-patients and 62,000 out-patients were treated at this hospital which constituted a record. The maintenance cost increased by £5000 and last year for the first time for seven years there was a deficit on the year's workings. Of the £167,000 needed for the enlargement, which is now practically completed, only £10,000 is still to be raised.

PROGNOSIS

A Series of Signed Articles contributed by invitation

XCVII.
PROGNOSIS OF TROPICAL SPRUE

THE syndrome of tropical sprue is explicable in terms of a metabolic breakdown of the gastro-intestinal tract characterised by malabsorption in the small intestine of such substances as fat, calcium, and glucose, and defective secretion of Castle's *intrinsic* factor. Whether this breakdown is related to primary dietary deficiency or is dependent on some underlying endocrine disturbance is unknown. The view of Castle and his colleagues, based on observations in Porto Rico, that deficiency of *extrinsic* factor in the diet is responsible for sprue is not in accord with experience of this disease acquired in other parts of the tropics. In India, for example, both Hindus and Moslems living on diets deficient in extrinsic factor develop tropical macrocytic anæmia, whereas the well-to-do European, who enjoys a diet containing adequate sources of extrinsic factor, such as red meat and eggs, acquires sprue. Similarly in Africa, when disease develops associated with a diet deficient in extrinsic factor, it is tropical macrocytic anæmia and never sprue which results.

Like pernicious anæmia, tropical sprue shows a natural tendency to remission and relapse, and in the tropics, before modern treatment was practised, it generally terminated fatally from (1) asthenia and uncontrollable diarrhœa with or without tetany; (2) profound megalocytic anæmia; (3) intestinal ulceration and perforation; (4) intercurrent disease. On the other hand, if the patient suffering from the disease could afford to return to Europe and underwent treatment which included prolonged bed rest and an initial dietary of low calorie value, recovery was not infrequent, provided the scales were not weighted against the patient by excessive age or intercurrent disease.

PROGNOSIS FOLLOWING MODERN TREATMENT

Granted the coöperation of the patient and the absence of intercurrent disease, patients with tropical sprue both in the primary attack and in relapse are now almost invariably restored to health by modern treatment. This treatment aims at restoring alimentary function and reinforcing demonstrable deficiencies and consists of (1) adequate bed rest; (2) a series of graded diets high in protein,* adequate in vitamin, and low in fat and carbohydrates; (3) liver extract in adequate dosage for a sufficient period administered by the oral or parenteral route or by both; (4) calcium salts per os reinforced in some instances by vitamin D. Liver extract is not nearly so effective when given alone; unless combined with a strict dietary it often fails to relieve alimentary symptoms and anæmia.

As a routine patients should continue liver extract therapy for 3 months in doses equivalent to 1½ lb. daily for the first month, 1 lb. daily for the second month, and ½ lb. daily for the third month. A high protein type of diet including cooked liver and plenty of fruit and vegetables should be adhered to for at least 6 months after freedom from symptoms. Condiments are to be avoided and the carbohydrate and fat intake only gradually increased. If there is a history of repeated relapses or any doubt regarding complete restoration of the blood to normal, an adequate maintenance dose of liver extract should be advised, the oral dosage being generally equal to ½ lb. whole liver daily or injections of Campolon (6 c.cm.) each week for another 3 months or longer if indicated.

* The calorie value of these diets varies from 700 to 3000 per day and the ratio of protein : fat : carbohydrate is approximately 1·0 : 0·3 : 1·3. Either meat (Trans. Roy. Soc. Trop. Med. and Hyg., 1930, xxiv., 131) or milk casein (Ibid., 1932, xxv., 297) may constitute the source of protein.

INDICES TO RECOVERY

Clinical features.—The clinical effects of combined treatment are very obvious. The stools rapidly decrease in bulk and number and assume a normal colour and consistency. Abdominal distension and intestinal flatulence disappear and the appetite improves; cramps and tetany cease. The nutritional state of the body becomes more satisfactory; the skin assumes a normal colour and consistency, and the nails lose their brittleness. The patient puts on weight, becomes contented and cheerful, and in a period of some 8 weeks is free from symptoms and on the high road to normal health.

Hæmatological findings.—Provided the alimentary features are controlled by an adequate diet the response to liver extract per os (equivalent to 1½ lb. daily of whole liver) is efficacious in restoring the blood picture to normal in at least 90 per cent. of cases. A maximal reticulocyte response occurs from the sixth to the tenth day and rapid blood regeneration follows. The blood loses its megalocytic characteristics as judged by the Price-Jones curve, and normal blood counts are generally established within 2 months of beginning treatment. In gravely anæmic patients, where an early maximal response is urgently required, oral liver therapy should be reinforced with daily intramuscular injections of 6 c.cm. of campolon or another suitable preparation. A submaximal reticulocyte response and sluggish blood regeneration following the oral administration of liver suggest insufficient dosage, and are an indication for large doses of liver given parenterally (campolon 6–12 c.cm. daily). The failure may arise from (1) malabsorption; (2) insensitiveness to liver extract, a larger dose being required to get a given effect; (3) the presence of complications.

Biochemical data.—With cessation of diarrhœa and the reappearance of normal stools, the total fæcal fat decreases, the serum calcium increases, and the glucose-tolerance curve tends to assume a normal contour. Similarly, after the administration of glucose intravenously, normal curves are found, showing that the sluggish utilisation of sugar has disappeared. The fractional test-meal in most instances also shows an improved acid secretion, though many months or even years may intervene before the curve resumes its normal shape. That secretion of intrinsic factor by the pyloric and Brunner's glands is also restored is beyond doubt, for, unlike sufferers from pernicious anæmia, many patients who have had sprue and recovered maintain a normal blood picture on a normal diet.

FACTORS INIMICAL TO RECOVERY

Various factors inimical to recovery, such as age, the presence of complications and of intercurrent disease, call for consideration.

Age.—Tropical sprue is exceedingly rare under the age of 20 years, and formerly patients contracting the disease during the third or fourth decades were regarded as having much better prospects of cure than those developing it later in life. With modern

treatment, however, old age per se does not necessarily affect the prognosis adversely; it is the concomitant degenerative cardiovascular or renal changes and intercurrent infection common to this period of life which make for anxiety. Of five patients over 70 whom I have had under observation during the past three years, only one has failed to respond satisfactorily; that patient is over 80 years of age and suffers from an enlarged prostate and *B. coli* cystitis; only temporary improvement has followed treatment in his case. Two others relapsed mildly but immediately responded to another course of treatment.

Intestinal ulceration and other complications.—Ordinarily the course of sprue is afebrile, but occasionally fever develops, and when it does so it is a warning signal suggestive of intercurrent disease or intestinal ulceration. The latter may be suspected from the presence of pathological exudate or occult blood in the stools, and calls for rigorous restriction of carbohydrates and fat, as distension of the bowel may lead to perforation, peritonitis, and death. Similarly, thrombosis of the cæcal veins may follow hypotension and intestinal distension and lead to local rupture and general peritonitis. Neuritis and tetany are two of the commoner complications. Both conditions clear up as the general health improves. Occasionally tetany persists, and here fat analysis will always show persistent steatorrhœa. If fat is further eliminated from the diet and the fat content of the fæces reduced to a normal level, calcium is adequately absorbed and hypocalcæmia and tetany rapidly disappear. Vitamin D and ultraviolet irradiation may be of assistance under such circumstances.

Intercurrent disease.—Cardiovascular degeneration, thyrotoxicosis, sepsis, respiratory infections, and *B. coli* infections of the genito-urinary tract are conditions which militate against recovery. Their existence may be reflected in a submaximal reticulocytosis and sluggish production of erythrocytes or hæmoglobin. The presence of hypochromia always suggests intercurrent disease, as does also undue lag in the production of hæmoglobin following liver extract therapy at a time when erythrocytes are being satisfactorily produced. Iron in full dosage is indicated for hypochromia, and the possibility of associated ankylostomiasis and amœbiasis must receive special attention.

Lack of response to modern treatment suggests either that the condition is not tropical sprue or that complications or intercurrent disease exist. In their absence health should be restored and no patient should to-day succumb to this disease. The position is quite the reverse with the idiopathic steatorrhœa of cooler climates, where therapy holds out little prospect of success.

RELAPSE AND CURE

The question of when a patient with sprue is cured is more easily asked than answered, for patients may recover from the primary attack and remain perfectly well in a non-endemic area as long as 7 years before relapsing with typical features. Statistical information is not yet available on the relapse rate, but many patients have remained well for periods up to 5 years following the treatment outlined. On the other hand, some relapse repeatedly after becoming apparently fit. Mental worry, poverty and all that it entails, indiscretions of diet, chill, and respiratory infection are factors tending to precipitate relapse. Sore tongue, abdominal flatulence, and looseness of the bowels, especially in the morning, are danger signals and indications for rest in bed and appropriate treatment. The therapeutic response in relapses is just as satisfactory as in the primary attack.

RETURN TO THE TROPICS

An attack of sprue used to be regarded as a definite contra-indication to return to the tropics. Nowadays patients who have recovered may be allowed back provided (1) they have remained free from all sprue symptoms for 6 months on a normal diet; (2) the hæmatological and biochemical findings are normal throughout this period; (3) they are otherwise healthy and are under 55 years of age.

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MEDICINE AND THE LAW

A Reasonable Income-tax Deduction

THE annual requirement of the filling up of income-tax forms is an opportunity for recalling a fact with which every medical practitioner may not be acquainted. The inspectors of taxes allow it to be known that the practitioner is entitled to deduct the cost of his annual subscription to a defence society when computing his professional profits for assessment under Schedule D. Where a doctor is assessed under Schedule E in respect of salaried employment, the deduction is not allowed unless membership of a defence society is a condition of the holding of the appointment. While it is not the purpose of this note to commend any particular society, it is reasonable to remind practitioners that valuable benefits accrue from membership of such bodies and that the cost of the subscription is deemed by the Inland Revenue a necessary expense for the conduct of a practice.

Local Authority and Sale of Diseased Meat

In an astonishing case at the Clerkenwell police-court lately the corporation of the borough of Swindon was fined £10 (with an order to pay £10 10*s.* costs) for sending to London for purpose of sale two hind-quarters of beef which were unfit for human consumption. Last February the Wiltshire county veterinary inspector had to deal with a cow suspected of tuberculosis. On his report to the local authority the existence of the disease was confirmed by the Swindon veterinary inspector and the animal was slaughtered. The Swindon inspector examined the carcass and condemned the offal and forequarters (which were destroyed) but apparently regarded the hindquarters as good enough to be sold for human food in London. Fortunately the sanitary inspector for Finsbury detected the transaction. He found the meat affected by generalised tuberculosis and quite unfit for human food. It was condemned on a magistrate's order. In the Clerkenwell proceedings there was an uncomfortable suggestion that the Swindon officials were anxious to relieve the rates of the incidental expense of compensating the farmer and of dealing with the case. It was not, of course, the fact that the officials themselves stood to profit in any way. The local authority, under the Tuberculosis Order of 1925, became the owner of the meat. It is a horrible idea that a local authority may have a financial interest in marketing diseased food. The Ministry of Agriculture will doubtless consider the possibility of stopping this disgusting traffic.

SPECIAL ARTICLES

BRITISH CONGRESS OF OBSTETRICS AND GYNÆCOLOGY

(*Concluded from p. 865*)

Dr. DOUGLAS MILLER presided at the morning session on April 2nd when Dr. J. HEYMAN described the

Radiumhemmet Methods and Results in Cancer of the Corpus

He said that the difficulties of presenting statistics on corpus cancer related mainly to (1) its distinction from the other forms of uterine carcinoma, (2) the requirements with regard to the histological diagnosis, (3) the criteria determining which patients should be regarded as "symptom-free." These criteria were rigid at the Radiumhemmet. Cases were regarded as symptom-free only if there was both an objective and a subjective cure after five years. Written reports from the patient were useless without examination because she might feel well and yet have a carcinoma of the body of the uterus. She must feel well, be able to work, and show no palpable changes due to cancer. The standard dosage given to fundus cases was now 1500 milligramme-element hours for each of two treatments. There was no risk of rupturing the uterus in packing it, but it was sometimes difficult to remove the radium because the cervix contracted. It should therefore be anchored by strong ligature. Tests with various ligatures had been made, and Irish linen thread proved the strongest. (Applause.) Many cases of carcinoma of the fundus were combined with other forms of carcinoma, notably of the cervix or of the ovaries. The figures presented concerned only cases of carcinoma of the fundus alone. It was very difficult to attain international uniformity of classification, but it should be possible if the pathologist attached to the clinic verified every diagnosis. At the Radiumhemmet between 1914 and 1930 inclusive, 232 cases of corpus cancer had been examined with a view to treatment. Of these, 224 were treated, and had been observed for at least five years. With radiological treatment, and operation in cases of failure, an absolute cure-rate of 42·2 per cent., and a relative cure-rate—i.e., in cases treated—of 43·7 per cent., had been obtained. The relative cure-rate of the cases treated radiologically only was 33 per cent. The series included 37·9 per cent. clinically operable cases, 44·6 per cent. technically operable, and 17·4 per cent. inoperable cases. The relative cure-rate obtained in these three groups was: 55·3, 41, and 25·6 per cent. respectively, cases operated upon being included, and 41·2, 30, and 23·1 per cent. respectively, cases operated upon being excluded. In comparing the Radiumhemmet results with those obtained by surgery, the absolute cure-rate could not be used as a basis for comparison, because the initial material in the surgical and radiological series was not uniform. Conclusions from a comparison of the relative cure-rates in operable cases had to be drawn with the greatest care because of the small number of cases, particularly in the radiological statistics. Another way had been tried to find an answer to the question of operative versus radiological treatment in operable cases. In the years under review 63 cases of corpus cancer had been referred to the Radiumhemmet after radical operation, and had been submitted to post-operative radiation. Fifty of these cases were alive and symptom-free five years after treatment, thus giving a five-year cure of 79·4 per cent. In this cure-figure, which was nearly twice as high as for those mainly radiologically treated, Dr. Heyman found support for the view that cases of corpus cancer suitable for operation should be operated upon. Meanwhile, the radiological methods of treatment should be improved. At the Radiumhemmet since 1930, a new method of intra-uterine application for treating corpus cancer had been adopted. The uterus is packed with a number of radium tubes each placed in a separate small lead capsule. Dr. Heyman described the calculation of the dosage, a new method of packing the uterus, and the technique of application, and reviewed the early results obtained with this method.

Dr. GRAY WARD agreed that classification was a great difficulty. In a joint corpus and cervix case there was a tendency to assume the growth had begun in the cervix if it were of the adeno-type, but this was not necessarily so. The absolute cure-rate was the only real criterion of results, and he defined this as the relation between the number of the cases who applied to the clinic for treatment and the number of those who survived. He emphasised the value of a personal follow-up, which was achieved in New York in at least 90 per cent. of the cases. Dr. Heyman's cases were registered by the Government and it was therefore possible to have 100 per cent. follow-up. There was an increasing tendency to prefer a ten to a five years time limit, and patients lost sight of within that time must be assumed to be dead of cancer. Dr. Gray Ward's favourite technique in the treatment of carcinoma of the fundus was hysterectomy, preceded by radium one month earlier, and followed by deep X ray treatment.

Mr. MALCOLM DONALDSON said that the radio-sensitivity of malignant disease of the corpus must be considered. Dr. Heyman had implied that the treatment was a purely physical problem—viz., the insertion of enough radium, but while the radio-sensitivity of cervical carcinoma was very high that of corpus carcinoma was very low. He had once left radium in the uterus for 14 days, and had then done a hysterectomy, when comparatively little change was found in the uterus.

Prof. C. G. LOWRY said he had had very little experience of radiotherapy, as he operated on practically all operable cases. He had had encouraging results, however, in a few technically inoperable cases. He had long thought that the association of corpus and cervical carcinoma was commoner than statistics suggested. The field for operation was widening owing to better anæsthesia and the introduction of blood transfusion.

Prof. R. J. JOHNSTONE assumed that Dr. Heyman only advocated the packing method of inserting radium when the body of the uterus was dilated.

Prof. FARQUHAR MURRAY said he had stopped operating for carcinoma of the fundus. He asked for details of post-operative radiation, and wondered whether it delayed healing.

Prof. MILES PHILLIPS said he operated whenever possible. He wondered whether carcinoma of the isthmus should be regarded as a special type, for it appeared to be particularly virulent, and operative results were poor.

Dr. HEYMAN, in reply, said that he was not convinced that there was any difference between the

radio-sensitivity of corpus and of cervix carcinoma. He thought that the reason why adeno-carcinoma was considered less radio-sensitive was that it was usually a rapidly spreading tumour. Cases of adeno-carcinoma of the cervix usually fell into groups 1 or 4 because metastases formed very rapidly. The principle in radium treatment was to cover the entire surface of the tumour with radium. He had not much use for deep X rays, but he occasionally employed them if there was any recurrence after radium. He agreed that his new packing method was only applicable in cases where there was a large uterus. It was difficult to diagnose cases arising in the isthmus without operation; in attempting to ascertain the origin of the disease he curetted the cervix and then passed ring forceps into the body. He looked upon the growth as combined only if tumour material was collected both by the ring forceps and the curette, not if subsequent curettage revealed growth in both positions.

Prof. GILBERT I. STRACHAN then reviewed the possibility of

Uterine Carcinoma following Radiotherapy for Benign Lesions

He reported two cases in detail, in which radium was applied for benign uterine bleeding, and the absence of carcinoma was established microscopically; amenorrhœa followed, but in one case two and in the other seven years later carcinoma of the body of the uterus followed. Prof. Strachan discussed the action of radium, on the uterus or on ovarian tissue, also the differences of morphology in corporeal and cervical epithelium after the menopause. He concluded that there was no evidence to show that the radium was in any way causative of the carcinoma. The fact that radium did not shield the patient from later carcinoma was no justification for reverting to hysterectomy in these cases, as the operative risk would be greater than the very slight possibility of subsequent carcinoma.

Mr. PERCY MALPAS read a communication on

Radium in the Treatment of Uterine Bleeding

based upon nearly 200 cases of benign uterine bleeding treated with radium in Liverpool and available for after-study. He discussed the subject under the headings: (*a*) mode of action of radium, (*b*) technique, (*c*) permanent amenorrhœa, (*d*) control of bleeding with conservation of menstrual and reproductive function, (*e*) other lesions of the uterus. The results obtained depended upon a combination of the action of the radium upon both the endometrium and the ovaries, but the only readily calculable effect was that upon the endometrium. Once a certain critical point of endometrical reaction, such as was certainly obtained with a dose of 2500 mg. hours, was attained, then the ovaries, even if incompletely irradiated, could not restore menstruation and would undergo a secondary degeneration, as happens in cases of hysterectomy with ovarian conservation. In cases where the endometrium had received a submaximal dose, the possibility of ultimate restoration of function depended upon the degree of ovarian reaction to the radium. As regards technique, he considered that the use of intra-uterine radium had outstanding advantages over other routes. The most important point in the technique was the exclusion by preliminary curettage of an early carcinoma of the uterus, since otherwise by the use of a sub-lethal dose a fibrous reaction might be set up masking its presence until it was too advanced for treatment. Essen-Moller had had malignant change appearing later in the uterus in 6 cases out of 200 despite an initial curettage, and for this reason had given up the method, and one similar case had been encountered in the present series. Mr. Malpas held that the occurrence of such cases did not invalidate the value of the method of radium castration, but emphasised the need for thoroughness in its technique. It must be remembered that curettage might not reveal growth, but pyometra or watery discharge following irradiation should be looked on as suggesting malignancy and be treated by hysterectomy.

For the production of permanent amenorrhœa the simplicity and certainty, the freedom from undesirable systemic reactions, and the opportunity it affords of a confirmatory curettage, made it preferable to X ray sterilisation. The use of radium in sub-menopausal dosage to control bleeding with conservation of menstrual and reproductive function had a definite scope, the main limitation of the method being its uncertainty. There was no special age limit, but most patients were at menopausal age. Precautions to be taken before treatment was undertaken were the exclusion of gross inflammatory appendage disease, and the presence of fibroids if submucous and pedunculated or degenerating, or larger than a three months' pregnancy. The total dosage given was 1500 to 2000 mg. hours, rarely 2500 mg. hours. In the Liverpool series of cases the mortality was *nil* and there were no injuries. Thirty cases (16 per cent.) continued bleeding up to ten weeks. Post-irradiation carcinoma occurred in 0·6 per cent. There was late return of transient bleeding in 4 per cent. and menopause symptoms in 23 per cent. Failure to control bleeding occurred in 4 cases (2·2 per cent.). The disadvantages of temporary control of bleeding were uncertainty of dosage, the possibility of uterine scarring, and the permanent impairment of reproductive functions. In submaximal doses the effect was chiefly on the ovaries. A dose of 600 mg. hours should not be exceeded for this purpose. The risk of cervical stenosis leading to dystocia was only very slight if the dose was less than a carcinoma dose. There was probably no risk of fœtal lesions following *pre*conceptional irradiation. Despite much inquiry it was still uncertain whether the primary effect of radium was on the ovaries or on the endometrium. Probably if permanent amenorrhœa was produced, there was an irreparable change in endometrium whatever the effect on the ovaries, because if the dose was big enough the bleeding *never* recurred.

Miss L. MARTINDALE read a paper on the treatment of

Uterine Hæmorrhage in Non-malignant Disease

with special reference to the choice of surgical operation versus irradiation by radium or X rays. She said that in deciding upon the best type of treatment for each individual case it was of primary importance: (1) to diagnose the cause of the hæmorrhage and the physical signs, (2) to consider the age of the patient and the degree to which future capacity for child-bearing was important to her, (3) to have in hand a full report of her general health. With regard to (1), Miss Martindale's study had been confined to hæmorrhage caused by metropathia hæmorrhagica, selected cases of uterine myomata, and functional, idiopathic, or essential hæmorrhage.

Surgical operation, either abdominal myomectomy (the operation of choice in young patients) or hysterectomy, was performed in 54·07 per cent.

of Miss Martindale's series of 762 cases. The case-mortality rate varied from 1 to 3 per cent., depending upon the type of operation and general condition of the patient. *Irradiation* was performed on 45·93 per cent. of the cases (radium treatment 9·19 per cent., deep X ray therapy 36·74 per cent.) with no mortality. Miss Martindale described the technique used by her with radium and with deep X rays. The advantages of radium treatment over operation were, briefly, the conservation of uterus and ovaries, and in many cases also of their function; and the short time spent in hospital and short convalescence. The disadvantages were nausea, occasional continuance or reappearance of bleeding, leucorrhœa (the "bestrahlungs" endometritis), and the possibility of acute nephritis. Also a case-mortality rate according to various observers of between 0·3 and 2 per cent., deaths being due to acute peritonitis or acute purulent salpingitis. Other disadvantages included the possibility of a future pregnancy, and, in that case, the effect of radium in causing stenosis of the cervix and obstruction of labour; further, the direct effect of radium on the fœtus (microcephalic idiocy). Cases were cited to illustrate these points. The conclusion was drawn, however, that preconception irradiation in non-malignant cases with few exceptions leads to no difficulties in labour, but that should a fibrosed cervix cause obstruction, Cæsarean hysterectomy is indicated.

Deep X ray therapy Miss Martindale regarded as a specific in all cases of metropathia hæmorrhagica or small interstitial fibroids. She emphasised the importance of an exact technique with careful calibration of X ray tubes and apparatus. Of 280 cases treated only 3·5 per cent. were not cured by X rays alone. There was no death in this series. In four cases hysterectomy was performed subsequently for malignancy, one 15 years after for carcinoma of cervix, one 7 years after for carcinoma of fundus, one 3 years after for carcinoma of fundus, and one 5 years after for sarcoma of fibroid. The risk of malignant disease occurring in an irradiated uterus was thus no greater than the risk in an untreated case. Miss Martindale cited mass statistics of several thousands of cases in support of her thesis that X ray treatment was superior to radium treatment. X ray therapy had no mortality, produced no resulting complications, and there was no fear of a stenosed cervix or of the stirring up of a latent adnexal inflammation. Radium therapy was, however, preferable to X ray therapy in very anæmic patients, in whom a quick cessation of hæmorrhage was important; in these cases a blood transfusion was indicated and a diagnostic curettage imperative.

Dr. HEYMAN said that there was no sharp limit between benign and malignant tumours of the ovary, and that possibly the same applied to uterine carcinoma. He thought, therefore, that the cases reported of carcinoma following treatment might have been due rather to failure in the pathological diagnosis than to subsequent development of carcinoma. As an example, he referred to a patient, aged 40, who was twice treated with apparent success by radiotherapy for large fibroids; on her return on a third occasion she was curetted and carcinoma was found.

Prof. FARQUHAR MURRAY recalled four cases of cancer following radium treatment for non-malignant conditions, and thought their presence must have been overlooked at the time. He said that 87 per cent. of cases of non-malignant uterine lesions were cured by radium, and that he always inserted radium if possible after curetting. He did not agree that contra-indication to radium should be limited to *gross* pelvic inflammation; in his view it was very risky to use it if the patient had any pain at all. He also doubted the wisdom of using radium for a fibroid as large as a four months' pregnancy.

Dr. GRAY WARD thought that the failure of radium in certain cases might be due to unsuccessful anchorage of the tubes. He always threaded a stitch through the cervix and secured it at the vulva.

Mr. MALCOLM DONALDSON thought it was unjustifiable to treat a patient under the age of 40 by radiotherapy, because it was impossible to foretell the effect on the ovaries. Radiotherapy might lead to extreme menopause symptoms even in quite small dosage. The great objection to treating large fibroids by this method was that it was impossible to say whether inflamed tubes were present.

Dr. G. W. THEOBALD wondered how Prof. Strachan and Miss Martindale had satisfied themselves that radium and X ray treatment did not increase the tendency to subsequent development of carcinoma. He thought all cases should be followed up for 30 years, and then compared with the general incidence of cancer in the country.

Prof. DANIEL DOUGAL, referring to Dr. Malpas's paper, said that he used a dosage of 2000–2400 milligramme hours; 94 per cent. of his cases either had no further bleeding at all, or only during the first week or so. Flushes were present in 75 per cent., and 83 per cent. said their general health had improved. He agreed that the action of radium was very largely on the ovaries, and that it was therefore probably better to do a subtotal hysterectomy in young people.

Prof. STRACHAN could not agree that curettage was an imperfect way of examining the cavity of the uterus. It was likely that most of the patients under consideration, and the gynæcologists now present, would be dead in 30 years' time. He did not think that the action of radium was on the ovaries. He had known two patients, aged 20 and 24, die of functional uterine hæmorrhage.

Miss MARTINDALE, in reply, said she was grateful to Dr. Gray Ward for his suggestion of anchoring radium. She agreed that X rays were useless in very young women because it might be quite impossible in these cases to get amenorrhœa. She had never seen X rays do harm in the presence of inflamed tubes, but radium might be very dangerous in such cases. She agreed that the action of radium was not on the ovaries. X rays acted on the ovaries, but only on the Graafian follicles, and not on the interstitial cells.

At the afternoon session, Prof. STRACHAN presiding, Dr. GEORGE GRAY WARD spoke on

Reconstructive Pelvic Surgery for Genital Prolapse

He showed an interesting series of lantern slides, demonstrating among other things the importance of retaining the uterus in an anteverted position, to prevent the intra-abdominal pressure from forcing the bladder down. He said that all forms of genital prolapse must be discussed together, as they were usually associated in varying degrees. Where prolapse of the uterus itself existed it must always be corrected, or whatever operative procedure was employed—e.g., for cystocele—would be unsatisfactory. For the cure of prolapse of the uterus, the principle of reefing the base of the broad ligaments—the cardinal ligaments of the upper pelvic floor—by approximating them in front of the cervix (or its stump if

amputated), thus elevating and anteverting the uterus by throwing back the lower pole of the organ, was a sine qua non if the uterus was to be retained in its normal position and condition for future childbearing. This basic principle was common to various techniques; to Donald of Manchester belonged the credit for first appreciating and employing it definitely in 1888. That the principle of the so-called "Manchester operation" was sound was not open to dispute, but Dr. Ward believed that in certain cases it should be supplemented by shortening the round and uterosacral ligaments, in order to restore all the supports and steadying apparatus that have been overstretched in a prolapsed retroverted uterus. Furthermore this technique did not fulfil the requirements in *all* cases; for women past the menopause and sometimes in younger women other types of operation might be more suitable and equally satisfactory. Dr. Ward outlined some of these and reported results of operations for genital prolapse at the Women's Hospital, New York. No one operative technique, he said, was suitable for all cases. The surgeon must individualise each case and utilise the appropriate technique to correct all the defects. Approximately 95 per cent. cures could be obtained by appropriate means. It was only advisable in very rare cases to combine abdominal with vaginal operation, since this added to the mortality and morbidity of the operation. The Watkins' interposition operation was good in suitable cases; it was better than colporrhaphy in resisting stress in old women. A preliminary curettage should always be done to exclude malignancy. The Mayo operation of vaginal hysterectomy was valuable for procidentia. What remained after amputation of the cervix was practically useless. The uterosacral ligaments must be shortened and the floor of the pouch of Douglas removed to prevent enterocele. Dr. Gray Ward described his own modification of Mayo's operation. Results were very difficult to compare, since there was no agreement about time limit for cure. At Dr. Ward's clinic there had been an organised follow-up since 1918; 94 per cent. of his own cases showed satisfactory results.

Prof. FLETCHER SHAW found that any relapses were almost always due to enterocele. He did not find it necessary to do any operation other than the Manchester one, although very rarely there was so little muscular tissue in the vagina that it was necessary to combine the operation with abdominal fixation. After the menopause 97 per cent. of cases were cured of their symptoms. He only removed the uterus if it was diseased and said that in such a case the repair must be done with particular care if recurrence was to be avoided.

Prof. MILES PHILLIPS said that in young women it was sometimes best to combine a moderate anterior colporrhaphy with Gilliam's suspension. He considered enterocele was best treated by some plastic procedure after hysterectomy. He favoured combined vaginal hysterectomy with repair of prolapse.

Dr. C. KAUFMANN read a paper on the

Clinical Uses of the Female Sex Hormones

He said that follicular hormone was responsible for formation of genitalia and had an effect on the whole body, while corpus luteum hormone prepared the uterus for pregnancy and maintained the pregnancy. When *dosage* was under consideration it must be remembered that the results obtained from investigations on castrated women did not necessarily apply to healthy women. The results of deficiency of ovarian follicular hormone were (1) primary amenorrhœa in which the genitalia might be undeveloped or normal and (2) secondary amenorrhœa. It was useless to try to produce *spontaneous* menstruation with follicular hormone. In secondary amenorrhœa it was essential to exclude extrinsic causes such as pulmonary tuberculosis. The results of treatment of this condition on the whole were poor, for though follicular hormone was uniformly successful in producing menstruation, this only continued in 25 per cent. of cases when the treatment was stopped. These results would probably be improved if follicular hormone were combined with corpus luteum hormone. Blood transfusion, with blood of pregnant women, was done in 14 cases of secondary amenorrhœa last year, of which 50 per cent. continued to menstruate. For sterility follicular hormone was only valuable if there were signs of deficient ovarian function—6 out of 7 such cases in Dr. Kaufmann's series had children. The type of hormonal hæmorrhage which led to repeated miscarriage might be arrested by the administration of corpus luteum hormone. His practice was to give 10 mg. of corpus luteum hormone daily for five days. For menopausal hæmorrhage, where carcinoma had been excluded, 2 mg.[1] of corpus luteum hormone should be given daily for five days. Threatened miscarriage and habitual abortion could be stopped by corpus luteum hormone, 10 mg. injected weekly, with a double dose during the week in which the period should have come. Ovarian therapy gave good results in climacteric disturbances; it relieved flushes, cardiac neuroses, and psychological disturbances, but objective evidence of activity must always be looked for. On pruritus vulvæ, with or without ulceration, at the menopause, follicular hormone had a marvellous effect. Dr. Kaufmann showed convincing coloured pictures of very severe senile ulceration of the vulva at the menopause, before and after treatment. He also described a case of amenorrhœa with pruritus where irritation ceased and menstruation returned after three weeks' treatment. It would be of interest to ascertain whether follicular hormone cured idiopathic neuritis at the menopause. He warned members of the congress not to expect too much, and to use hormone treatment in a rational manner.

Mr. T. N. A. JEFFCOATE spoke on

Organotherapy for Functional Uterine Hæmorrhage

He said that before 1930 whole gland preparations used empirically, usually by the mouth, were almost devoid of biologically active principles. His present communication was only concerned with therapeutic agents of standardised biological activity. In attempting to assay the results of the treatment of functional uterine hæmorrhage with these substances he had collected the results of over 500 cases recorded between 1930 and 1935; made inquiry into the immediate and remote results of 80 cases, treated in Liverpool since 1932, and hitherto unpublished; and considered views expressed by foreign authorities in reply to a questionnaire. The conclusions reached were that the use of œstrin was theoretically unsound. Corpus luteum and gonadotropic hormones were equally efficacious, but they were of greater value in the treatment of puberty bleeding than in the control of hæmorrhage occurring later in life. These

[1] One international unit of progestin (corpus luteum hormone) = the activity of 1 mg. crystalline progesterone standard. This is approximately equivalent to 4 German clinical units and to 1 to 1½ rabbit units hitherto quoted for progestin. 1 mg. of corpus luteum hormone therefore = 1 international unit.

hormones controlled the immediate hæmorrhage, but it was doubtful whether they had any action in re-establishing a subsequent regular menstrual cycle. "Anovular" bleeding, commonly associated with endometrial hyperplasia, gave the best response to this form of organotherapy, which adequately controlled hæmorrhage in two out of every three cases. It was difficult to assess the value of hormone preparations because two different observers might describe the results in the same case, one as "no response to treatment," and the other as "cured." In a collected series, only 68·7 per cent. were cured, and many relapsed. The best results with antuitrin S (gonadotropic hormone) were obtained at puberty. Of those treated at puberty, 77·7 per cent. were cured; at ages 20 to 40, 61·2 per cent.; and after 40 only 50 per cent. The best results were obtained with metrostaxis, the worst with epimenorrhœa. The dosage was 1 c.cm. daily till bleeding ceases. Unless the bleeding was cyclical it was useless to inject except when the patient was actually bleeding. Relapses did not yield so well to treatment as did the primary condition, possibly owing to the formation of antihormones, but this was not proved.

Additional short papers on this subject were read by Dr. P. M. F. Bishop, Dr. Gregor, and Prof. E. C. Dodds. Prof. DODDS stressed the danger of attributing too much significance to urine and blood analyses in these cases. These hormones were just as real as thyroxine—viz., *real chemical entities*. The only reason that the results were not better was that their use was not yet understood. Dr. BISHOP said that his experience at the Endocrine Clinic at Guy's Hospital corresponded closely with that of Dr. Kaufmann and Mr. Jeffcoate. Small doses, 1000 international units of follicular hormone daily by mouth, might control the flushings of the menopause. The dose should be kept as low as possible because care was necessary in withdrawal. Injections should only be given if oral treatment had failed. He confirmed the fact that good results would be obtained with pruritus, but warned members that this treatment might cause alarming temporary swelling of the vulva. The recent synthesis of progestin was a very great advance and had led to a reduction in price.

On April 3rd, the concluding day of the congress, papers were read by Dr. Leonard Colebrook (Prevention of Puerperal Sepsis), Dr. H. R. MacLennan (Contracted Pelvis in Scotland), and Dr. G. W. Theobald (Relationship between Pregnancy and Chronic Nephritis).

UNITED STATES OF AMERICA

(FROM AN OCCASIONAL CORRESPONDENT)

CASE FINDING IN TUBERCULOSIS

YOU have recently (March 7th, p. 561) drawn attention to the use of tuberculin tests with X ray follow-up of positive reactors as a routine method in the Scandinavian countries for early diagnosis of pulmonary tuberculosis. The same method is now in use in the United States. It is being tried on a State-wide scale in New Mexico where three organisations have pooled their resources in order to extend the early diagnosis campaign, not only to every institution of higher learning in the State but also, so far as is practicable, to senior high school students as well. The Mantoux test, using the new P.P.D. tuberculin, is given to all students. A single X ray chest film is taken of all those who react positively. Coöperating in this survey are the New Mexico Bureau of Public Health, the Maztag Research Laboratory of the South-western Presbyterian Sanatorium, and the New Mexico Tuberculosis Association. The survey is regarded not only as a public health measure for early diagnosis but as an interesting project in clinical research. For more than a generation now health seekers in all stages of pulmonary tuberculosis, and from all parts of the United States, have flocked to New Mexico in the expectation that its climate would enhance their chances of recovery. Hundreds of these pilgrims have indeed recovered and now direct the business and take a large part in the professional activities of the State. Thousands, of course, lie buried in New Mexico cemeteries, and of these less is remembered than of the more fortunate survivors. Probably no one will ever know whether and to what extent climate has contributed to the quota of those who regained their health. But another question presents itself: What is to be the effect of this mighty pilgrimage upon succeeding generations of New Mexico citizens? A survey made two years ago showed that whereas twice as many English-speaking (i.e., in the broad sense immigrant) citizens suffer from active tuberculosis as do the Spanish-speaking (indigenous) citizens, nevertheless among the children of the former only one-half as many react positively to the Mantoux test as among the children of the indigenous group. The present study is expected to tell what is the heritage of early adult type tuberculosis among the generation of offspring who have at present reached undergraduate age. It will also tell the cost of this method of case-finding in the undergraduate age-group.

Ulster county, New York, has developed a very economical method of case-finding by X ray. They first use the fluoroscope on positive reactors and then subject suspicious chests to photography. The proportion of films used to cases fluoroscoped is 11 per cent. Up to November of last year 8000 tuberculin tests had been given, 1956 fluoroscopic examinations made. This last figure represents 652 grade school-children positive to the tuberculin tests, and 804 parents of these children, together with 500 high school-children. The cost of discovering active tuberculosis has averaged $7 per case. Four cases were found in the grade school group, 6 in the high school group, and 26 among the parents. In addition 18 "suspicious" cases were recorded and 29 non-tuberculous but pathological conditions were discovered. This investigation in Ulster county, N.Y., has now progressed into its fourth year.

TRENDS OF MORTALITY

Complete returns in last year's mortality are not yet available, but all indications point to another year of low mortality. Indeed, the wage-earning population as represented by the 17 million policy-holders of the Metropolitan Company in Canada and the United States have achieved an all-time low record of 8·4 per 1000. It is a remarkable fact that the rate in this group has been 7 per cent. lower in the depression years 1930–35 than it was in the prosperity years 1924–29. The tuberculosis death-rate last year reached 55·6 per 100,000, a reduction of 6·4 per cent. below the previous low record in the previous year. Again it is remarkable that the tuberculosis death-rate should have continued its decline among wage earners throughout the depression and even declined at an accelerated pace. Death-rates from diarrhœal diseases, chronic nephritis, and causes incidental to childbirth also reached new minima. Rates for cancer, diabetes, and heart

diseases were lower than in 1934. The death-rate from alcoholism is the lowest in many years; there has been a marked decline since the repeal of prohibition.

SCOTLAND

(FROM OUR OWN CORRESPONDENT)

THE HEALTH OF SCOTLAND

THE seventh annual report of the Department of Health for Scotland, which has just been published, shows a general death-rate of 13·2 per thousand, which is slightly higher than last year's. The maternal mortality-rate was 6·3 per thousand births, which approximates to the average for the past five years. The urgent need of improvement in the standard of midwifery is emphasised and it is apparent that the need for antenatal supervision is not sufficiently realised by the general public. The number of deaths of infants under one year of age again reached a low record rate (76·8 per thousand births). The general health of the population was maintained, but the incidence of sickness among insured persons remains high, there being a total of over 18,500,000 days of unfitness for work among insured persons. The output of houses by local authorities was 18,651, which was the highest ever achieved in Scotland. Of these, 15,000 were built under slum clearance schemes.

THE "EDINBURGH MEDICAL JOURNAL"

The current issue of the *Edinburgh Medical Journal* records the resignation of the editor, Mr. Alexander Miles. For no less than 25 years Mr. Miles has skilfully supervised its publication and has maintained a high scientific and academic standard. As a surgeon, teacher, and administrator he has done important work and his long and successful editorship constitutes a further service to medicine of which the members of the Edinburgh school are highly appreciative. Dr. A. Rae Gilchrist, who takes over the duties of editor, has our best wishes for the prosperity of the journal.

It is 131 years since the *Edinburgh Medical and Surgical Journal* was issued as a quarterly magazine under the editorship of the younger Andrew Duncan. In January, 1841, the *Edinburgh Monthly Journal of Medical Science* made its appearance. Later in the same year its name was altered to the *London and Edinburgh Monthly Journal of Medical Science*, and in 1846 it became simple the *Monthly Journal of Medical Science*. The latter was amalgamated with the *Edinburgh Medical and Surgical Journal* in 1855, and in July of that year the *Edinburgh Medical Journal* made its first appearance as the successor to both the periodicals. The first editor was Henry Duncan Littlejohn, professor of medical jurisprudence. A further alteration in the journal has been that since 1922 the transactions of the Medico-Chirurgical and Obstetrical Societies have been published within its covers.

NEW FACILITIES FOR OPHTHALMOLOGY

The late Dr. Gavin Paterson Tennent, formerly a physician to the Western Infirmary, Glasgow, directed his trustees to pay over to the University of Glasgow a sum sufficient to found a chair of ophthalmology, and also allocated a sum to provide, in connexion therewith, a suitable building at the Infirmary. The new ophthalmological department thus established, which has cost £45,000, was opened last week. It is in charge of Prof. A. J. Ballantyne and is to become a centre of higher study and research. It should be of great value since it will provide opportunities for advanced study in ophthalmology which are at present not easily obtained.

A PUBLIC ASSISTANCE MEDICAL SERVICE

A new medical service for the poor has been set up in Clydebank. Since 1930 the service has been carried on by dividing the burgh into three districts and appointing a part-time officer for each. The number of visits and consultations in a year has been about 12,500. Under the new scheme a panel of 14 local practitioners has been formed and these will be paid, according to the number of visits and consultations made during the year, from a pool of £900 to be divided annually by the town council.

IRELAND

(FROM OUR OWN CORRESPONDENT)

COMPULSORY RETIREMENT OF THE OFFICERS OF LOCAL AUTHORITIES

A FEW weeks ago the Minister for Local Government and Public Health of the Irish Free State issued to all local authorities throughout the country a circular letter in which he advised them that officers in their employment should normally be compulsorily retired at the age of 65, and that in some cases, examples of which were given, the retiring age should be 60. As a retiring age was not mentioned in the terms of appointment of any of the officers concerned, much discontent was roused, and some doubt expressed as to the powers of the local authorities to compel retirement. The Minister has been asked in the Dáil to quote the statutory powers possessed by local authorities which would enable them to follow his advice, but he did not respond. He admitted that his circular was not an order, but merely a recommendation, a point which had been misunderstood by many of the local authorities. Further questioned as to whether a local authority had power to retire an officer compulsorily on the ground of age alone, he replied that other circumstances would be taken into account. Last week it was reported in the daily press that the central council of the Local Government Officials' Union had taken the opinion of senior counsel as to the legality of the Minister's action. The opinion of Mr. M. J. Ryan, K.C., as quoted in the press, was to the effect that the action of the Minister was ultra vires and that the circular need not be acted on by local authorities, as there was no law by which compulsory retirement could be enforced. Should the department advise a local authority to retire an official on reaching the age of 65, the authority could refuse to do so, and the only step then open to the department would be to call for the retirement of the official on the grounds of incompetency or incapacity, and the whole circumstances would have to be investigated. Counsel's opinion, as quoted, does not appear to deal with the situation which would arise if the local authority were willing to follow the Minister's advice, but the officer refused to retire. It seems unlikely that the Minister should have acted without making sure of the legal position, but his reluctance to answer questions in the Dáil suggests that he is not quite satisfied on the point. Should the compulsory retirement be made effective it will press hard on medical men who had entered public service relatively late in life, for the pension depends on the number of years' service.

PROGRESS OF PHYSIOTHERAPY

A LUNCHEON was held at the Langham Hotel, Portland-place, on April 8th, in connexion with the coming International Congress of Physical Medicine to be held on May 12th–16th. Lord Horder presided and took the opportunity of making a presentation to the principal guest, Dr. Richard King Brown, medical editor of the *British Journal of Physical Medicine*, in recognition of his services to physiotherapy. Lord Horder gave a short account of Dr. King Brown's career—his ten years as medical officer of health in Bermondsey, the foundation in 1926 of the first municipal solarium in London, his translations of notable German works on his specialty, and, latterly, his arduous work for the *Journal*. Referring to the Sixth International Congress, he said that the decision to hold it in London was a tribute to the work of the English group and would give a great fillip to the march of physical medicine in Great Britain. The help and sympathy received from the Foreign Office and from the Ministry of Health had been very valuable, and 30 of the 35 countries invited had already accepted. He himself had the privilege of being honorary president of the Congress, but he very much regretted that he would not be present, because some time before the dates had been arranged he had accepted an invitation to visit America.

Lord Horder said that he had advocated the claims of physical medicine in season and out of season. He welcomed the Congress because it would stimulate this growing branch of preventive and curative treatment. Physiotherapy was not a new form of medicine; he believed that it was the oldest, for when Adam delved it was the first attempt to keep fit, though psychotherapy might claim Eve's spinning as the first contribution making for equanimity. It was only recently, however, that control had become absolutely essential. The wealth of methods and apparatus almost made him hope that nothing more would come, to allow breathing space to test and prove the means already available. Physical medicine went on from strength to strength; its achievements had been considerable, its potentialities were incalculable. The pitfalls, however, were perhaps more and deeper than in any other branch of medicine. The greatest was the temptation, enhanced by the public's faith in machinery, to apply it indiscriminately to all types of disease. There was also the danger of the physiotherapist losing touch with the physicist on the one hand and with the clinician on the other. Ideally, of course, he ought to be both but he ought still to look for guidance and support from each; he had much to teach them, but he had also much to learn, and there was no end to learning. Another danger was that he might wander from the bed-rock of pathology and lose himself in the sea of speculation; or, worse, he might construct a pathology of his own, which could only be a pseudo-pathology. There was, lastly, the peculiar danger that he might be commercialised by the astute business man. The only real safeguards from these pitfalls were those that applied to all branches of medicine—namely, the integrity of the practitioner; colleagueship and all that it implied; the group spirit, which was essential to advance; and the opportunities given for free discussion, criticism, and the dissemination of knowledge and improved technique. The Congress would help to establish these.

Dr. King Brown replied, thanking the president for his tribute and for the presentation. He had begun his work of editing the *British Journal of Physical Medicine* with little knowledge of journalism and its success, he said, was due to the help he had received. It was the only one of its kind in the English language.

Sir Francis Fremantle proposed a vote of thanks to Lord Horder and said that the coming Congress would be a valuable contribution at this time to international peace and goodwill.

PANEL AND CONTRACT PRACTICE

Fitness for Work: Who Decides?

Dr. A, an insurance practitioner in Scotland, certified a patient to be unfit for work. The approved society referred the case to the regional medical officer who certified him not unfit. The man again consulted Dr. A who advised him to try some light form of work, but the patient decided not to do so and appealed to the Scottish Department of Health against the R.M.O.'s decision. In the meantime, pending the result of the appeal, Dr. A continued to issue certificates of incapacity. In due course the medical service subcommittee considered the matter and according to the *Journal* of the National Association of Clerks to Insurance Committees "decided that the insurance practitioner should not have given unfit certificates after the regional medical officer had given a contrary opinion." Eventually the committee decided that the doctor had failed to comply with the terms of service and recommended a deduction of five guineas from his capitation fees. If the facts are as stated this decision is extraordinary. What probably happened is that the decision against Dr. A was taken because he had given certificates of incapacity after he had himself concurred in the R.M.O.'s opinion of the case to the extent of advising the patient to try some light form of work. The functions of the R.M.O. in relation to incapacity for work are advisory, and the responsibility for deciding whether a certificate of incapacity should be issued or not rests with the insurance practitioner. If he is honestly of the opinion that the patient is incapacitated for work, even though the R.M.O. is of contrary opinion, the practitioner should continue to certify if the patient so requests. Whether benefit should be paid or not rests not with him but with the approved society.

A Distinction Without a Difference

A case recently reported to an insurance committee has attracted considerable attention in the lay press. An insured person, who was a maid in the employ of a lady of title, had been suffering from quinsy, and Dr. B upon whose list her name appeared had attended her until Saturday, Feb. 29th, on which date he visited her twice. On the Sunday Dr. B received a telephone message requesting him not to call that day. On the Monday he called at the house and was informed by the housekeeper that he could not see the patient, whereupon he gave the housekeeper to understand that it was necessary that he should do so. Dr. B was then told that if he did not go away the police would be called in, and he, therefore, communicated with the insurance committee stating that he could not hold himself responsible for the patient's treatment. The

committee wrote to the employer recapitulating the facts and pointing out that an insurance doctor is required by his terms of service to visit at his or her place of residence any patient whose condition so requires, but that owing (it would appear) to the housekeeper's attitude Dr. B had been prevented from fulfilling his obligations. The employer was invited to offer any observations she might deem proper on the circumstances. A letter received from the employer's private secretary indicated that the first time the secretary saw Dr. B she "distinctly told him that, as Her Ladyship wished the patient to have the very best attention, he need not treat her as a panel patient but as a private patient, and to send a note of his fees, in due course, which if he will do in respect of the calls he made, he will be paid at the ordinary medical rate." The letter went on to say that subsequently the patient wished to be seen by the family doctor and upon the employer's instructions his services were requisitioned.

There is no reason to doubt that in this case the employer genuinely wished to do the best thing possible for her employee, but it is unfortunate that what was described, at the meeting of the insurance committee, as the atmosphere prevalent at the commencement of the last reign, should still be in evidence. Under Clause 8 (1) of the terms of service, the treatment which a practitioner is required to give his patient comprises all proper and necessary medical services other than those involving the application of special skill and experience of a degree or kind which general practitioners as a class cannot reasonably be expected to possess. Moreover, under Clause 10 (1), a practitioner is not permitted to demand or accept any fee or other remuneration in respect of treatment which he is required to give under the terms of service. The report of the subcommittee which dealt with the matter notes the employer's view that the medical treatment available under the Act is inferior to that which a person would receive if treated as a private patient. It also notes that the reports submitted to the insurance committee from time to time with regard to the treatment provided by insurance practitioners for insured persons—e.g., the nature of medicaments and preparations ordered at the cost of insurance funds—should go far to dispel the idea that there is any difference between what is popularly known as "panel treatment" and that which a private patient would receive. A letter has been sent to the employer pointing all this out and deprecating her action, taken doubtless in ignorance, in having invited the practitioner to treat an insured person on his list as a private patient. It rests with insurance practitioners themselves to demonstrate that there is no difference between the treatment provided for their insured patients and that provided for their private patients.

OBITUARY

ALFRED MASON VANN, M.R.C.S. Eng., L.S.A.

Dr. Alfred Vann, for many years medical officer of health for Durham City, was born in Durham and began his medical training as a student at the local hospital, but proceeded for its later stages to King's College Hospital, London, where he obtained a Warneford scholarship. He qualified as M.R.C.S. Eng., L.S.A. in 1883, but did not complete his university course although he took honours in the preliminary scientific and intermediate M.B. Lond. examinations, while he also gained the silver medal in botany from the Society of Apothecaries, London. He began practice in Durham nearly fifty years ago and promptly made his mark, holding within a short space of time a local post under the poor-law as medical officer and public vaccinator, then surgeon to the Durham City Constabulary, and then surgeon to the Durham County Hospital. Simultaneously with these appointments he was elected medical officer of health for the city, a post which he held for 34 years, resigning in 1918 but retaining his position of medical inspector of school-children under the city education committee. He also took charge of the X ray and electrotherapeutic department of the county hospital where on retirement he was appointed consultant. Dr. Vann was a man of considerable accomplishments. He had edited certain sections of "Bentley's Botany," he contributed interesting cases to the *Transactions* of the Northumberland and Durham Medical Society, and had marked artistic talents. He was 75 years of age.

SIDNEY ISAAC PRITCHETT, L.R.C.P. Lond., M.R.C.S. Eng., D.P.H.

Dr. Sidney Pritchett, who died recently in Rochester, was born in the old cathedral city and educated at King Edward's School, Birmingham. He received his medical training in Birmingham and at St. George's Hospital, qualified in 1890, and held several resident appointments at Queen's Hospital, Birmingham. He was for a time in the P. and O. service, but went into practice in Rochester nearly forty years ago and soon became a prominent civic official. He was appointed full-time M.O.H. for the city in 1902, school medical officer, and medical officer to the city and port. He was also surgeon to St. Bartholomew's Hospital, Rochester, and medical officer to the Rochester and Chatham Joint Hospital (the St. William's Hospital). He resigned these posts in 1934, having thus been in charge of the city's health services for 32 years, and was the recipient of gratifying public appreciations. He was a bachelor and 70 years of age at the time of his death.

BRITISH EMPIRE CANCER CAMPAIGN.—The 58th quarterly meeting of the grand council was held in London on April 6th, when it was announced that the King had been pleased to become patron of the Campaign. Invitations to become members of grand council were extended to, among others, Lady Barrett, M.S., and Sir David Wilkie, F.R.C.S. The following grants, amounting to £5530 and making a total to date of £30,990 for the year 1936, were approved: £1100 to the Radium Beam Therapy Research; £1750 (in addition to the grant of £1850 already made for the year 1936) to the Mount Vernon Hospital; £500 (in addition to the grant of £600 already made for the year 1936) to the Marie Curie Hospital; £100 and £80 to Dr. C. R. Amies, at the Lister Institute, and Dr. P. R. Peacock, of Glasgow, respectively, for the purchase of special types of centrifuges; £1000 to the Manchester Committee on Cancer to cover the cost for two years' investigations into the possible connexion between the use of heavy oils in motor vehicles and the apparent increase in the incidence of cancer of the upper air-passages and the lungs; £1000 to the North of England branch of the Campaign to meet the cost for the second year of the short-wave investigations being carried out at Newcastle, on behalf of the Campaign, under the direction of Prof. W. E. Curtis and Mr. F. Dickens, D.Sc.

Notification was received that the Royal Society and the Medical Research Council had nominated Prof. Matthew Stewart to succeed Prof. R. T. Leiper, F.R.S., who has retired, as one of their five nominees on the scientific advisory committee of the Campaign.

CORRESPONDENCE

PROPHYLACTIC ENUCLEATION OF LOWER WISDOM TOOTH FOLLICLES

To the Editor of THE LANCET

SIR,—In my lectures before the Royal College of Surgeons [1] I have produced the evidence of 622 case-reports of abnormality and complication of the third molars in support of my contention that, cramped as they are for room in the modern jaw, these teeth when mal-erupted constitute a definite clinical menace. The mandibular tooth is responsible for much the greater number of complications as well as the larger proportion of grave ones. The abnormality is dental—but the complications are medical and surgical. They range from severe and incapacitating neuralgias of one or other of the branches of the trigeminus to grave spreading infections involving the cavernous sinus or the mediastinum and ending in death. I have produced, as well, evidence not only of the severity of the operation for removal of this tooth, when buried or impacted, but also of the gravity of the post-operative complications, which range from ununited fracture of the jaw to fatal septicæmia.

FIG. 1.—Skiagram of a male, aged 21, showing the type of impaction which may be expected to result if the germ of the wisdom tooth shown in Fig. 2 continues to maturity.

FIG. 2.—Skiagram of a female, aged 9½, showing the germ of the wisdom tooth already badly inclined in the "impacted position." This also shows the latest optimum stage of development at which enucleation is best performed.

[1] Arris and Gale lecture (Feb. 21st, 1934), THE LANCET, 1934, i., 416; Hunterian lecture (Feb. 9th, 1935), Ibid., 1935, i., 313 and 463.

It became obvious that a great deal of unnecessary suffering would be saved if a prophylactic measure could be devised to eliminate the risks attendant upon mal-eruption. A critical study of a large mass of osteological material, correlated with the radiograms of children and young animals arranged in growth series, made it plain that probable impaction of the lower wisdom tooth could be assessed with great accuracy from 9 to 11 years of age, and that the removal of the whole dental follicle with the embryonic tooth, if it could be accomplished satisfactorily, would be a desirable prophylactic operation. So far as I can trace I am the first person to attempt this operation, the simplicity of which I announced in my former lecture (Feb. 21st, 1934), when I showed a slide of the technique. I hope to publish the operative details in due course, but surgical colleagues who have seen it have urged me to make this preliminary announcement now that I have completed 70 cases.

FIG. 3.—Skiagram of the same patient as Fig. 2 a year and 10 months after operation, showing obliteration of the dental crypt by ossification.

The operation is exceptionally free from trauma if made early enough. The small wound inside the mouth heals by first intention and the children leave the ward on the following day. This contrasts most favourably with the trauma and long convalescence involved in operating on the fully developed misplaced tooth (Fig. 1). The operation is, however, essentially one of surgery rather than of dentistry. Fig. 2 reproduces a skiagram showing a suitable case in a child of 9½ years. The crown of the wisdom is beginning to calcify in such an oblique angle that normal eruption could not be expected. The third skiagram (Fig. 3) shows the same case 22 months after operation. Obliteration of the dental crypt has proceeded satisfactorily. The molars in front have not been injured or disturbed.

I am, Sir, yours faithfully,

London, W., March 30th. C. BOWDLER HENRY.

MENTAL HYGIENE IN MENTAL HOSPITALS

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The appearance of finely granular casts does not seem to be any contra-indication to continuing the treatment. I have never found it accompanied by albuminuria or oliguria, and the casts are frequently absent from the next specimen of urine which is examined, even though the administration of mandelic acid is continued. Moreover, as Holling and Platt point out, the treatment apparently has no deleterious effect in cases of nephritis or nephrosis.

In a series of 26 cases, most of which were under the care of Mr. E. W. Riches at the Middlesex Hospital, I have found so great a variation in the amount of ammonium chloride required to keep the pH of the urine between 5·0 and 5·3, both in different patients and during the course of treatment of a single patient, that I doubt whether any combination of mandelic acid or its salts with the non-specific acidifying agent will prove entirely satisfactory. While 6 or 8 grammes of ammonium chloride is the usual daily dose required, I have had one patient for whom 1·5 g. was sufficient, and others who required 10 or 12 g. One patient's requirements varied from 4 to 12 g. during the course of treatment. Of Holling and Platt's three adult cases treated with ammonium mandelate, in only one was the recommended dose of mandelic acid (12 g. a day, or four doses of 51 grains of ammonium mandelate) given with no additions. In order to obtain the correct pH in the other cases, in one the dose of mandelic acid was reduced below the amount recommended, and in the other ammonium chloride had to be added. The tendency of ammonium chloride to produce anorexia, indigestion, nausea, and occasionally vomiting, is certainly a grave disadvantage in a few cases, though I have never had to stop treatment on this account. If the claims made for Gelamon are not exaggerated, this preparation of ammonium chloride may solve the problem. It is swallowed in the form of tablets which swell up into a gelatinous mass in the stomach; this is slowly dissolved and absorbed without giving rise to any disturbance of gastric function.

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The agitation was eventually successful and it brought not only repeal of the Acts but sweeping changes of the English law in regard to sex morals. Moreover, it led to improvements in the Service conditions which have brought venereal diseases down from 267 cases per 1000 men in 1886 to 10 per 1000 in 1933. These and many other changes for the better we celebrate on April 23rd and 24th. Lady Astor, Prof. Gilbert Murray, and two descendants of Josephine Butler, Mr. R. A. Butler, M.P. (Under-Secretary for India), and Mr. Andrew Butler, will speak at the public luncheon at the Criterion on the 23rd, which will be followed by a service of thanksgiving at St. Martin-in-the-Fields at 6 P.M. at which the Bishop of Liverpool will preach a special sermon. Tickets and further particulars of the meeting on the 24th can be obtained at this office.

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Great Britain never had the full continental system of registered women and licensed houses, but it made a beginning between 1864–69 with the C.D. Acts and introduced the "registered prostitute," under special police control and regular medical inspection, for use of the Army and Navy in certain garrison towns. The object was to reduce venereal diseases in the Services but the results were nil. We now know that such medical examination of one sex only for the benefit of the other does not protect the other; but it was not known then, or not generally accepted, by the medical profession and the officials. A certain small number of doctors and administrators did criticise the Acts for medical reasons, but the deep and passionate revolt against them came from men and women who opposed them not only on moral grounds but primarily on grounds of the gross violation of the principles of law and justice involved in the Acts. Mrs. Butler warned the people of this country:

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Mr. FORT complained of the delay in introducing the fresh unemployment assistance regulations.—Mr. BATEY said that he would not be satisfied with the abolition of the household means test. He stood for the abolition of the family means test and the personal means test as well.

Mr. GUY said that the great justification for an inquiry into special circumstances was that some special provision might be made in cases of particular need. Everyone knew that there were cases of hardship under the present means test. There should be a distinction between the standard of assistance given in this case and that given under the poor-law. They did not want a destitution test for the able-bodied unemployed. They wanted a certain standard of living for them, so that they might be maintained as efficient units ready to take their place again in industry.

REPLY BY THE MINISTER OF LABOUR

Mr. ERNEST BROWN said that the problem could be simply stated, but it could not be simply solved. The trouble was that the new system was applied to thousands of towns and villages where an infinite variety of practice had previously reigned. They had to consider the effect of the regulations and to see how they could meet what fair-minded people would regard as genuine hardships. Those investigations were almost at an end, and what the Government put in their election manifesto they meant to carry out. The House would not have long to wait. His own impression was that the local area officers were doing their work extraordinarily well, with a great understanding of the circumstances of those who came to them, with great sympathy, and with a desire to do what the Act intended—namely, to make the new system a more humane means of dealing with the able-bodied unemployed. It was easy to urge the abolition of the means test and to bring forward hard cases. He had been surprised in the last nine months, not at the number of hard cases, but rather at the smallness of the number. They had to face the issue whether they ought to give public assistance without consideration of the question of means. There were two points—was there to be a test at all? and what kind of test was it to be? There had been many investigations into the question of whether or not there could be another test of need, and with one exception each investigation had come to the conclusion that if there was to be a test of need regarding applicants for public funds it must be in terms of the household. Whereas some local authorities administered State funds with the same care as that with which they administered their own ratepayers' money, there was another class of local authority that did not. The Government would do their best, and that very soon, to bring before the House improved arrangements for administering a uniform system with due regard to local opinion over the whole of Great Britain. The investigations were nearly complete and the House would not have to wait long after Easter.

HOUSE OF COMMONS

TUESDAY, APRIL 7TH

Poison Gas in Warfare

Mr. CARY asked the Secretary of State for War what type of training, if any, was carried out by the War Office in the use of poison gas as a legitimate weapon of warfare; and if chemical experts were employed to work to this end in consultation with Army authorities.—Mr. DUFF COOPER replied: No training in the use of poison gas as a weapon of war is carried out in the Army, but possible methods of the use of gas have naturally to be studied in connexion with training in defence against gas. Chemical experts have, of course, been closely associated with Army authorities in connexion with such training.

Mr. SHINWELL asked the Secretary of State for War the names and basis of the gases with which the anti-gas protectors for the troops had been recently tested; and whether the results had been proved effective.—Mr. DUFF COOPER replied: As I informed the hon. Member in reply to a question on 31st March last, the present pattern of mobilisation container is considered to provide adequate protection against the gases likely to be encountered. The hon. Member will doubtless realise that it is not in the public interest that I should answer the first part of his question.

Mr. SHINWELL asked the Secretary of State for War whether any protective clothing other than oilskins were in issue for the protection of the troops from corrosive and incendiary chemicals; whether he was aware that the German and other governments were now experimenting with rubber clothing.—Mr. DUFF COOPER replied: The answer to the first part of the question is in the negative, and to the second in the affirmative.

Mr. KIRKWOOD asked the Home Secretary whether the ability of infants and young children to breathe normally, if at all, in a gas mask had been satisfactorily established; whether the period of time was known that must elapse before gas lost its harmful effects when the populace could emerge from cover with safety; what was the penetrating quality of gas; was it capable of reaching those taking cover at, say, the underground railway level; and what action the Government proposed to take to prevent food and water, both under cover and otherwise, becoming contaminated by gas.—Mr. G. LLOYD replied: The question of the protection of infants and young persons is receiving attention and various alternative methods of protection are under investigation. The period of time during which poison gas continues to exercise its harmful effects depends upon a number of factors, such as the nature of the gas employed, the quantity liberated, and the meteorological conditions prevailing at the time. The instructions to be issued to the public will give advice as to when it is safe to emerge from cover. When poison gas is liberated it mixes with the air in the vicinity. This leads to a progressive dilution of the gas cloud which tends to follow the path of the normal air currents existing at the time. The question whether gas could reach the tube railways would depend upon the protective measures adopted in connexion with the supply of air to the railway. Consideration has already been given to this question. The Government have considered the action necessary to prevent food and water becoming contaminated by gas. Protective measures are quite practicable and will be embodied in the instructions to be issued to the public.

Sir GIFFORD FOX asked the Home Secretary whether he was yet in a position to make a statement about the supply of anti-gas respirators to the civilian population in case of air attack.—Mr. G. LLOYD, Under-Secretary, Home Office, replied: Yes, Sir. A simple but effective form of respirator, for use by the civil population, has been devised and the final design is now being settled. The Government propose to accumulate sufficient stocks of this respirator to enable issue to be made to all persons in areas exposed to danger in the event of air attack. The issue would be made free of charge. In the event of attack from the air everyone would be advised to remain indoors in a gas-proofed room in order to avoid danger of contamination; and the respirators for the use of the civil population would primarily be of service for the purpose of enabling people who were out of doors when a raid occurred, or whose gas-proofed rooms had been damaged, to get to a place of safety. The Government are fully alive to the need for providing for the needs of young children and babies, and special methods of protection are being developed for this purpose. It may be anticipated that many factories in this country will seek to put on the market respirators of their own design, and the Government have devised a scheme, the details of which are about to be published, by which manufacturers who make approved types of respirators and who accept various conditions, including liability to Government inspection, will be licensed to affix a Home Office certification mark to their respirators. Purchasers will be well advised not to regard respirators as satisfactory unless they bear this mark.

New Cost-of-Living Index Number

Mr. BOOTHBY asked the Minister of Labour whether he proposed to revise the basis of the cost-of-living index number.—Mr. E. BROWN replied: Yes, Sir, I have recently

given further consideration to this matter and have decided that a revision of the basis of the cost-of-living index number should now be undertaken. For this purpose, it will be necessary to collect data with regard to the distribution of the main items of expenditure of working-class households at the present time. An inquiry of this character, on a scale sufficiently comprehensive to provide representative information covering different seasons of the year, cannot be completed before the end of next year. In the meantime, the cost-of-living index number will continue to be calculated on the existing basis, and I anticipate that the new index number can be so linked on to the previous numbers as to continue the series without a break. I should add that as regards the methods to be adopted in the conduct of the inquiry, I hope to have the assistance of a small advisory committee which will include representatives of employers and trade unions.

WEDNESDAY, APRIL 8TH

Danger Spots and Road Accidents

Mr. ANSTRUTHER-GRAY asked the Minister of Transport if he could state from statistics of the last two years which were the three most dangerous spots in London, rural Scotland, and Glasgow, and the number of accidents that had occurred at each during that period.—Mr. HORE-BELISHA replied: The following statement shows certain streets in London and Glasgow in which road accidents involving personal injury have been particularly numerous. Information regarding accidents in the rural areas of Scotland cannot readily be given in this form:—

	Six months ended Sept. 30th—	
	1934.	1935.
LONDON—		
Sections of Commercial-road and East India Dock-road	236	251
Lewisham High-road and Eltham-road	158	155
Chiswick High-road and King-street	194	121
GLASGOW—		
Dumbarton-road from Church-street to Balshagray-avenue	121	128
Paisley-road and Paisley-road West, from Morrison-street to Lorne-street	92	97
Garscube-road, from Burnside-street to Possil-road	47	61

Sir ALFRED BEIT asked the Minister of Transport whether he would arrange for fuller publicity to be given regarding the ages and physical defects, if any, of the victims of road accidents.—Mr. HORE-BELISHA replied: Yes, Sir. The ages of persons killed and any physical defects from which they suffered, so far as they were considered to have been a cause of the accidents, will be shown in the Report on Fatal Accidents on the roads during 1935, which will be issued shortly. Similar particulars will be available in the reports on road accidents involving personal injury which are being obtained from the beginning of this month.

Captain STRICKLAND asked the Minister of Transport whether he had observed the reports of accidents to children cycling in the streets; and whether, when legislation was being introduced, he would consider fixing a minimum age for persons using bicycles, as was the case with motor cyclists.—Mr. HORE-BELISHA replied: Yes, Sir. The figures before me are alarming and show that nearly 40 per cent. of the cyclists killed in road accidents are under 21 years of age.

Out-patient Clinics for Mental Treatment

Mr. SORENSEN asked the Minister of Health the number of out-patient clinics for mental patients that had been established to the present date.—Mr. SHAKESPEARE replied: The latest available information indicates that there are now 143 out-patient clinics associated with public mental hospitals. More comprehensive particulars will be secured by a questionnaire which is shortly to be issued to local authorities by the Board of Control.

THURSDAY, APRIL 9TH

Maternity and Child Welfare

Mr. EDWARD WILLIAMS asked the Minister of Health whether he had been in touch with the British Medical Association with regard to maternity services; and, in view of their contention that a unified public health service was the most sure means of reducing maternal and infant mortality, what action he proposed to take in this matter.—Sir KINGSLEY WOOD replied: Yes, Sir. I have recently received a deputation from the Association on this subject. I stated that I should give further consideration to their proposals after I had received the report of my medical officers who are making special investigations in the areas in which the maternal mortality-rate is high.

PUBLIC HEALTH

Public-school Boys Learn About Public Health

ON the joint invitation of Sir Kingsley Wood, Minister of Health, and of Mr. Herbert Morrison, leader of the London County Council, a party of public-school boys and masters, 25 of each, spent three days in studying the problems of local administration in London. The qualification for admission of a boy was that he must have the school certificate and be over 17 years of age. In all 28 schools were represented. The party was welcomed by Lord Snell, chairman of the L.C.C., and then listened to an account by Mr. Morrison of the duties of the L.C.C. and how their functions are carried out by the various committees and departments. Dr. W. Allen Daley and Dr. Andrew Topping explained the work of the public health department, the former dealing with the broader aspects of hygiene. Dr. Daley told of the great epidemics of the past, of the work of the commissioners who investigated the conditions of life of the labouring classes nearly a hundred years ago, and of the rise and development of public health work. He described the environmental services, drains, sewers and sewage disposal, the collection and disposal of refuse, town-planning and building by-laws, the steps which are taken to ensure that houses are maintained in a satisfactory condition, and problems of unfit houses and clearance areas. And so on through the provision of pure air, pure water, and pure food, and the measures to control infectious disease, to the various medical services for the individual and the steps taken to educate the public. The importance of public health work to everyone was emphasised, examples being the economic burden to the community of the care of those who are disabled by mental or physical illness and of the dependants of those who prematurely die because of preventable illness. Mention was made of the epidemic which attacks rich and poor alike, of the serious effect which disease in our ports would cause to our shipping, and of the part played by medical discoveries in reducing the death-rate.

Interest was shown by the number and nature of the questions put to the lecturer. Only ten minutes had been allotted to questions, yet more than twice that time had to be given before the closure could be applied in order that the next item on the programme could proceed. Questions came almost entirely from the boys, the masters being interested to observe the first reactions of the boys to an address of this character. The first was an invitation to say what the next big development in public health work was likely to be. The answer hazarded in reply was that it might be a reorganisation of medical benefit as now provided under the National Health Insurance Acts so as to provide consultant and pathological services for insured persons and a medical

service for the dependants of the insured. The next questioner asked for a detailed description of the various grades of milk and, as a supplementary, an opinion on the nutritive value of pasteurised as compared with raw milk. Then came a question familiar to all lecturers on public health: what was the answer to the contention that modern hygiene was preserving the lives of the inefficient and the degenerate. From this it was an easy stage to a question what was being done for the mentally defective and what could be done to prevent the births of more mentally defectives; then euthanasia was raised and what doctors thought of it. Questions followed as to how the medical needs of the non-insured casual employed were provided, and what the L.C.C. was doing for the sleeper on the Embankment. Finally the lecturer's attention was invited to those just above the National Health Insurance level: what about the "black-coated worker" who had lost his job and who needed an operation?

In the afternoon the party divided into two groups and visited St. James's and St. Giles's Hospitals. On their return Dr. Topping addressed them on problems of hospital organisation and administration, after which he, too, was subjected to a barrage of questions. Dr. Topping referred to the provision made for the sick by the religious orders and the development from that of the great voluntary hospitals. He traced the provision made by the guardians of the poor for the destitute sick and showed that since 1929, when the old poor-law system was abolished and the work transferred to the councils, the hospitals were preparing to undertake every kind of medical treatment, particularly where, as in London, they had been "appropriated" from the poor-law and were now administered under the Public Health Acts. The two succeeding days were devoted to education and housing. The party was addressed by the valuer and the architect of the L.C.C., by a district inspector, and one of the assistant education officers. Visits were paid to various types of schools, to cottage housing estates, and slum clearance schemes.

INFECTIOUS DISEASE

IN ENGLAND AND WALES DURING THE WEEK ENDED APRIL 4TH, 1936

Notifications.—The following cases of infectious disease were notified during the week: Small-pox, 0; scarlet fever, 2232; diphtheria, 1134; enteric fever, 16; pneumonia (primary or influenzal), 1119; puerperal fever, 41; puerperal pyrexia, 121; cerebro-spinal fever, 27; acute poliomyelitis, 5; acute polio-encephalitis, 2; encephalitis lethargica, 8; dysentery, 27; ophthalmia neonatorum, 87. No case of cholera, plague, or typhus fever was notified during the week.

The number of cases in the Infectious Hospitals of the London County Council on April 10th was 6778, which included: Scarlet fever, 999; diphtheria, 1112; measles, 3284; whooping-cough, 648; puerperal fever, 14 mothers (plus 9 babies); encephalitis lethargica, 282; poliomyelitis, 5. At St. Margaret's Hospital there were 29 babies (plus 11 mothers) with ophthalmia neonatorum.

Deaths.—In 121 great towns, including London, there was no death from small-pox, 3 (2) from enteric fever, 81 (24) from measles, 10 (2) from scarlet fever, 32 (5) from whooping-cough, 29 (3) from diphtheria, 44 (15) from diarrhœa and enteritis under two years, and 71 (15) from influenza. The figures in parentheses are those for London itself.

The mortality from measles is still falling, the figures for the last eight weeks (working backwards) being 81, 104, 114, 105, 84, 88 78, 58 for the country as a whole, and 24, 38, 62, 58, 47, 38, 18, 14 for Greater London. Liverpool reported 7 deaths, Sheffield 6, Manchester 4, Gateshead 3, no other great town more than 2. Leeds reported 3 fatal cases of scarlet fever, Birmingham 3 of whooping-cough. Deaths from diphtheria were reported from 19 great towns, 3 each from Manchester and Sheffield.

The number of stillbirths notified during the week was 320 (corresponding to a rate of 49 per 1000 total births), including 49 in London.

MEDICAL NEWS

Royal College of Surgeons of England

A quarterly meeting of the council was held on April 6th, with Sir Cuthbert Wallace, the president, in the chair. The Jacksonian prize for 1935 was awarded to Mr. R. C. Brock, F.R.C.S., of Guy's Hospital, for his dissertation in the pathology, diagnosis, and treatment of intra-thoracic new growths, including neoplasms of the œsophagus, and a certificate of honourable mention and an honorarium of ten guineas was awarded to Mr. H. P. Nelson, F.R.C.S., of St. Bartholomew's Hospital. The subject for the Jacksonian prize for 1937 will be the pathology, diagnosis, and treatment of tumours of the pituitary gland.

The Walker prize for 1931–35 was awarded to Prof. E. L. Kennaway, M.D., F.R.S., of the Cancer Hospital, London, in recognition of the inspiration and direction he has given to investigations leading to the discovery of a pure chemical compound by which either carcinoma or sarcoma can be induced. The John Tomes prize for 1933–35 was awarded to Mr. Alfred William Wellings, M.D.S., for his original work on dental histology. The Cartwright medal for 1931–35 was awarded to Mr. Arthur Bulleid, M.R.C.S., L.D.S., of Guy's Hospital, for his essay on the relationship of pulpless teeth to general disease and their treatment, with special reference to periapical rarefaction. It was decided that the subject of the Cartwright prize for the years 1936–40 should be general and local diseases as factors in the causation of pathological oral conditions.

Reginald Seymour Lawrie, of Middlesex Hospital, was appointed Begley student for the ensuing three years. The president reported that he had appointed Mr. Sydney Scott as representative of the College at the International Congress of Laryngology, Rhinology, and Otology, to be held in Berlin in August, 1936. At the request of the director-general of the Indian Medical Service it was decided, subject to satisfactory arrangements being made, to hold a primary fellowship examination in India at the end of 1937.

Mr. H. L. Eason, vice-chancellor of the University of London, and Dr. Egbert Morland, assistant editor of THE LANCET, were elected fellows of the College under the charter which permits the council to elect annually to the fellowship without examination two members of twenty years' standing. A diploma of membership was granted to James Firth Heslop, of Manchester University.

Diplomas in child health were granted jointly with the Royal College of Physicians to the following candidates:—

Cécile H. D. Asher, L. I. S. Campbell, E. H. Capel, Meyer Carr, Anne A. Craig, R. H. Fish, Margaret L. Foxwell, S. C. Gawne, Constance M. Hall, Irene M. Holoran, A. H. Khan, Hah-Liong Lee, B. F. Longbotham, W. H. Patterson, Margaret R. Price, C. K. Rowan-Legge, W. I. D. Scott, J. M. Watt, and R. A. Wilson.

International Society of Medical Hydrology

The annual meeting of this society is to be held this year in Austria, from Oct. 10th to 16th. The opening ceremonies and the first medical discussion will take place in Innsbruck; the party will then proceed to Badgastein and Hofgastein, and go from there to Salzburg. After the meeting visits may be paid to the Salzkammergut and also to Vienna and Budapest. The two principal subjects for consideration are the spa treatment of disorders of old age, to be introduced by Sir Humphry Rolleston, and radio-activity in medicinal waters. A party will be formed to travel from London on Oct. 9th and non-members of the society may attend the meeting on payment of a small fee. Further particulars may be obtained from the general secretary at 109, Kingsway, London, W.C.2.

University of London

At the London School of Hygiene (Keppel-street, W.C.), at 5.30 P.M. on May 5th, 7th, and 8th, Prof. A. Butenandt, of the institute of organic chemistry at Danzig, will lecture on the biochemistry of the sterol group.—Mr. H. M. Traquair, ophthalmic surgeon to the Edinburgh Royal Infirmary, will give his (postponed) lectures on perimetry on May 18th and 19th at 5.30 P.M. at University College Hospital medical school.—On May 12th, 13th, and 14th, at 5.30 P.M., at the College of the Pharmaceutical Society (17, Bloomsbury-square, W.C.), Prof. Arthur Stoll, of Basle, will speak on cardiac glucosides.—On May 15th, at 5 P.M., at King's College, Strand, Dr. Henri Fredericq, professor of physiology in the University of Liége, will give a lecture on the laws of excitation of the autonomic nervous systems with reference to chemical mediators.—On May 21st Dr. Alfred Adler, of Vienna, will lecture on some developments in individual psychology; the meeting will be at University College at 5.30 P.M.—On May 7th and 8th, at 5.30 P.M., at the Royal Veterinary College, two lectures on mineral deficiency diseases of farm animals will be given by Prof. Henry Dryerre and Mr. J. Russell Greig, Ph.D.—Admission to the lectures is free, without ticket.

University of Adelaide

The South Australian Government has appointed Dr. E. Weston Hurst to be director of the new Institute of Medical Science which is being established in Adelaide.

Dr. Hurst, who is 35 years of age, graduated at Birmingham in 1922. He obtained the degree of M.D. two years later and of D.Sc. in 1932, when he also became M.R.C.P. Lond. In 1923–24 he was the Walter Myers travelling student of Birmingham University and he worked at the National Hospital, Queen-square, until in 1926 he was appointed pathologist to the Miller General Hospital, Greenwich. In 1928, for the Milbank Fund, he began investigations into poliomyelitis, and from that time he has been on the staff of the Lister Institute, holding the university appointment of reader in experimental pathology. From 1932–34 he was given leave of absence to work at the Rockefeller Institute at Princeton, New Jersey. His William Withering lectures, delivered at Birmingham and published in THE LANCET last September, formed an authoritative review of the neurotropic virus diseases, and his views on this subject are further expanded in the current issue of *Brain*. His own work includes original observations on the viruses of poliomyelitis and rabies.

Royal Faculty of Physicians and Surgeons of Glasgow

At a meeting of the Faculty, held on April 6th, with Prof. Archibald Young, the president, in the chair, the following were admitted to the fellowship:—

Edmund Denis Cooper, Thomas Neilson Fraser, Robert Sinclair Kerr, James Anthony Waring McCluskie, William John Brownlow Riddell, and Laurance David Wellwood Scott (Glasgow), Susilananda Sen (London), and Edgar William Thomas (Rhondda).

Royal College of Surgeons of Edinburgh

At recent examinations of the College the following candidates were successful:—

FINAL EXAMINATION FOR L.D.S.

Robert Lawrie, D. L. Mackenzie, Annie McA. Douglas, L. A. P. Cantin, H. R. Inglis, Elsbeth Gruneberg, E. O. Rossetti, Mary D. Shepherd, Kurt Bronne, Werner Sachs, and James Hughes.

Indian Medical Service

The annual dinner will be held at the Trocadero Restaurant, London, on Wednesday, June 17th, at 7.15 P.M., when Major-General Sir Robert McCarrison, C.I.E., will preside. Officers can arrange to sit near their friends, as separate tables to seat eight will be provided. Tickets from the joint hon. secretary, Sir Thomas Carey Evans, Hammersmith Hospital, Ducane-road, London, W.12.

Hunterian Society

At the annual general meeting of this society held on April 9th, the following office-bearers were elected:—

President: Mr. H. L. Attwater; vice-presidents: Dr. W. Brander, Dr. A. Westerman, Mr. M. Oldershaw, and Dr. W. H. F. Oxley; hon. treasurer: Dr. Irwin Moore; trustees: Sir Bruce Bruce-Porter and Dr. A. P. Gibbons; orator: Lord Horder; hon. secretaries: Mr. A. E. Porritt and Dr. John Leebody; members of the Council: Dr. Thomson Brown, Dr. S. Monckton Copeman, Dr. W. S. C. Copeman, Dr. G. R. Mather Cordiner, Dr. John Eyre, Dr. F. Howard Humphris, Dr. B. H. Jones, Dr. E. W. McCormick, Dr. W. Mailer, Dr. D. C. Norris, Dr. Basil Parsons-Smith, and Dr. A. Wilson; hon. librarian: Mr. A. E. Mortimer Woolf; auditors: Dr. Ernest Young and Mr. Andrew McAllister.

Prof. Grey Turner has been elected a corresponding member of the Surgical Society of Vienna.

King Edward's Hospital Fund for London

The King has signified his intention to give an annua subscription of £1000 to this Fund.

St. John Ambulance Brigade

The chief commissioner of the Brigade announces that he has appointed Dr. William C. Bentall to be his staff officer for air-raid precautions.

International Pædiatric Congress

This congress, which was to be held in Rome in September, has been postponed until the spring of next year.

Lectures on Nutrition

On April 21st, 22nd, 23rd, and 24th, at 6 P.M., Dr. J. Alison Glover will lecture at Gresham College, Basinghall-street, London, E.C. His subject is Some Aspects of Nutrition, and the lectures are open to all without charge.

West End Hospital for Nervous Diseases

A Savill prize is offered for the best thesis on a neurological subject submitted by a candidate who has attended the practice of this hospital on at least ten occasions. The subject chosen for the thesis should be submitted to the examiners not later than May 31st, and the thesis itself by Nov. 30th. Further information may be had from the secretary of the hospital, Welbeck-street, London, W.1.

Bayliss-Starling Scholarship

An award of this scholarship, which is of an annual value of £120, will shortly be made. The scholar will be required to follow a course at University College in the principle and methods of research in physiology and biochemistry. Further information is obtainable from the secretary of the college, Gower-street, London, W.C.1.

British Institute of Philosophy

The Wright memorial lecture, on the Romantic Factor in Modern Politics will be delivered by Prof. Ernest Barker at University College, Gower-street, London, W.C., at 5.45 P.M. on Thursday, May 7th. Cards of admission can be obtained from the director of studies at University Hall, 14, Gordon-square, London, W.C.1.

A Congress of Cardiologists

We are informed that a meeting of specialists in cardiology will be held at Royat over Whitsuntide (May 31st to June 1st), when the subject of discussion will be Vascular Spasm. British members of the foreign committee include Sir Thomas Lewis, F.R.S., Sir Farquhar Buzzard, Sir Walter Langdon-Brown, Sir Maurice Cassidy, Sir StClair Thomson, Dr. John Parkinson, Dr. F. W. Price, Dr. Basil Parsons-Smith, Dr. T. F. Cotton, Dr. Maurice Campbell, Dr. Evan Bedford, and Dr. A. P. Cawadias.

North Kensington Women's Welfare Centre

A lecture-demonstration on the theory and practice of contraception will be given at the gynæcological and birth control clinic on Thursday evening, April 30th, at 8.30 P.M. Dr. Helena Wright will be the lecturer, and a fee of 5*s*. is charged to meet the expenses incurred. There are daily clinic sessions at which further experience can be acquired and a fee of 1 guinea admits to two or three of these sessions as well as to the lecture-demonstration. Applications to attend the lecture and sessions should be made in advance to the secretary of the clinic, 12, Telford-road, Ladbroke-grove, W.10.

Rowett Research Institute

Dr. J. T. Irving has been appointed head of the physiology department of this institute, near Aberdeen, in succession to Dr. R. C. Garry who has become professor of physiology at St. Andrews.

Dr. Irving was born in Christchurch, New Zealand, and educated at Christ's College there. He came to England in 1920 as a student at Caius College, Cambridge, and was placed in the first class in both parts of the natural sciences tripos. From 1924 to 1928 he was engaged on research in biochemistry being awarded a Belt fellowship at Oxford during the last two of these years. In 1927 he received the degree of Ph.D. at Cambridge and in the following year he entered Guy's Hospital, London, to complete his medical studies. Since qualification in 1931 he has been lecturer in physiology at Bristol and Leeds. His investigations have been chiefly concerned with carbohydrate metabolism and with abdominal sensation.

PHYSICAL EDUCATION

THE report of the Physical Education Committee of the British Medical Association, published to-day by the Association and obtainable for the modest price of 6*d*., makes many important suggestions for the improvement of the physical efficiency of the nation. The Committee was appointed early in 1935 "to consider and report upon the necessity for the cultivation of the physical development of the civilian population and the methods to be pursued for this object." It consisted of 22 members, including the following 15 doctors: Dr. E. Kaye Le Fleming, Dr. S. Watson Smith, Mr. H. S. Souttar, Mr. N. Bishop Harman, Sir Henry Brackenbury, Mr. W. McAdam Eccles, Sir Crisp English, Dr. W. N. West-Watson, Dr. Adolphe Abrahams, Dame Janet Campbell, Dr. G. P. Crowden, Dr. Henry Herd, Dr. L. R. Lemprière, Mr. R. C. Elmslie, and Miss M. Forrester-Brown.

The Committee has received evidence from numerous expert witnesses and has circulated four different questionnaires which have been completed by schools, colleges, voluntary organisations and industrial firms, and representatives of foreign countries.

The report begins with a discussion of the importance of exercise, fresh air, sunshine, diet, clothing, and so forth in the maintenance of bodily fitness. This is followed by a survey of the position of physical education in the general educational system. The Committee finds that the existing arrangements in schools leave much to be desired. Usually too little time is devoted to the subject, and many schools possess neither suitable accommodation for gymnastic training nor sufficient playing field space for outdoor games.

It recommends that properly equipped gymnasia, together with changing rooms and shower baths, should be provided in senior elementary, central, and junior technical schools, and that facilities for games and swimming should be greatly increased. The importance of physical exercises being performed in appropriate costume is emphasised and local education authorities are urged to supply a stock of suitable clothing and gymnastic shoes for children who cannot provide their own. The appointment of expert organisers of physical education by all education authorities is strongly recommended and suggestions are made as to the numbers of organisers of both sexes required for different school populations.

The Committee deprecates the tendency, especially evident in many public schools for boys, to subordinate physical education in gymnasia to field games and athletics, and "to regard games as an unduly serious business rather than to play them for the pleasure of playing." It also condemns the practice, common in public and secondary schools, of curtailing the physical activities of senior pupils who are preparing for examinations. Instruction in elementary physiology and hygiene is considered to be an essential part of physical education and it is recommended that such instruction should be given in all schools as a branch of general science.

The provision made for the promotion of physical fitness among persons no longer attending school was found on investigation to be seriously inadequate. Despite the valuable contributions of local authorities, voluntary organisations, and business firms to the bodily well-being of this section of the population, it appears that at least 40 per cent. of persons between the ages of 14 and 40 take no part in organised physical recreation. It is recommended that the existing facilities should be greatly extended and that, as one means to this end, there should be closer coöperation between all organisations concerned with the physical welfare of the community. Hope is expressed that the recently established Central Council of Recreative Physical Training may act as an authoritative coördinating body, uniting in a common policy the endeavours of the Board of Education and the voluntary organisations.

The training of teachers of physical education is next discussed, and here the need is stressed for a greatly increased supply of men suitably trained to teach the subject in public and secondary schools for boys. The comparative neglect of physical education in the university training departments for teachers is deplored, and it is recommended that universities should not only provide for the physical education of undergraduates but should also establish an internal diploma in the subject.

Medical Supervision of Physical Education

Finally, the Committee envisages a much closer relation between physical education and the science and art of medicine. The recommendations (LV. to LXV.) arising from this aspect of their deliberations are set out in full below.

IN SCHOOLS

There should be close coöperation between the head master (or mistress), the school doctor, the parents, the gymnastic teacher, and the general teaching staff in all matters pertaining to the physical welfare of the individual pupil.

Such coöperation is especially desirable in the prevention of the strain which girls are liable to suffer in mixed schools.

Adequate medical supervision should be available to ensure that unfit children do not participate in unsuitable or excessive exercises or games and that undernourished children receive sufficient supplementary feeding to enable them to participate with benefit in the regular physical exercises undertaken by the other children.

IN VOLUNTARY ORGANISATIONS

There should be closer coöperation between the health services and the educational services, whether central or local, in relation to the physical education of the population. The medical and physical training staff of the local authority should be available for consultation in connexion with "keep-fit" and other recreative classes in the area.

Leaders should be trained to watch for signs of physical disability, and should advise any member of the class who appears distressed or unduly fatigued to consult his or her doctor before resuming attendance.

Clubs should attempt to provide suitable non-technical lectures, preferably by medical men, on physiology and hygiene.

Recreative physical activities provided by industrial firms should be linked with the medical supervision of the employees.

IN PHYSICAL TRAINING COLLEGES

Entrants to the physical training colleges should be subjected to a thorough medical examination.

Medical examinations of students in training at the physical training colleges should be held at frequent intervals, and the work of individual students regulated in accordance with the examination results.

The medical profession should coöperate with the gymnastic profession by investigating the physiological requirements and effects of the various exercises with a view to the scientific arrangement of the syllabus of training. To facilitate such investigation, efforts should be made to establish some uniform system of physical assessment of the individual student. In particular, a standard method of testing exercise tolerance should be devised.

Post-graduate courses should be established to provide

medical men and women with the special training which the medical supervision of physical education demands.

Appendices to the report contain an interesting historical sketch of physical education through the ages, a brief outline of the position of physical education in various foreign countries, and a description of a "standards" scheme for school athletics which is suggested as an alternative to the usual school sports system.

ROYAL MEDICAL BENEVOLENT FUND

At a recent meeting of the committee of this fund 13 new applicants were assisted and 41 grants were renewed to beneficiaries. In all £1398 was voted. The following particulars of a few cases helped indicate the kind of work undertaken.

M. B., 1933, aged 27, who was responsible for the maintenance of his mother and two younger brothers, had been prevented from taking up a salaried post owing to being in hospital for an operation and was without means. Fund voted £45.

L.R.C.P. Irel., aged 71. In 1935 he had a severe attack of hemiplegia, which affected his speech and legs. Although improved in health he has great difficulty in obtaining employment owing to his deafness, speech, and age. He is earning 10s. a week and is in receipt of the old age pension of 10s. a week. His wife was operated on in 1934 and is in a very weak state of health. She has the charge of a mentally defective daughter, and is endeavouring to increase her income by taking lodgers. Fund voted £40 per annum to the doctor and £26 to his wife.

Widow of medical man aged 67. Suffering from pernicious anæmia; has been operated for cataract and has lost one eye. On the death of her husband in 1936 she was left with her daughter in great financial difficulties, the only asset being the possible sale of the practice for £400. Two sisters-in-law, both in very poor circumstances, have given all assistance within their powers. Fund voted £26 per annum and a special gift of £10.

Widow of medical man aged 33, left on the death of her husband with three children aged 5, 2½ years, and 6 months, and a capital sum of under £2000. The Ladies' Guild will help with education.

Daughter of medical man aged 54, suffering from diabetes, has an income of £60 per annum. Fund voted £26 per annum.

This is the centenary year of the fund and a special appeal is being made for new subscribers to raise the annual income by subscriptions and donations to £20,000. From the present income of £14,000 allowances of £40 and £26 are made to medical practitioners and their dependents respectively. The increased income would enable the committee to raise these allowances to £52 and £36. An appeal is also being made this year for special donations to create a fund from which larger grants can be voted to very urgent and distressing cases, and which may be used to help with the training of widows and orphan sons and daughters of medical practitioners to enable them to be self-supporting. Cheques should be made payable to the hon. treasurer of the Fund, 11, Chandos-street, London, W.1.

LONDON AND COUNTIES MEDICAL PROTECTION SOCIETY LIMITED.—The annual general meeting of this society will be held at Victory House, Leicester-square, London, on Wednesday, May 6th, at 4 P.M., to receive and adopt the annual report and balance sheet, and to transact other business of the society.

INTERNATIONAL ASSOCIATION FOR PREVENTION OF BLINDNESS.—The general assembly of this association and of the International Organisation of the Campaign against Trachoma will be held at 3 P.M. on Monday, May 11th, at the Centre Marcelin Berthelot, 28 bis, rue St.-Dominique, Paris. Prof. de Lapersonne, the president, will take the chair, and communications will be made by Dr. Park Lewis, Prof. F. Terrien, Mr. R. P. Wilson, Mr. A. F. MacCallan, and Mr. Bishop Harman. Further particulars may be had from the secretary at 66, Boulevard Saint-Michel, Paris.

Medical Diary

SOCIETIES

ROYAL SOCIETY OF MEDICINE, 1, Wimpole-street, W.
TUESDAY, April 21st.—5.30 P.M. Meeting of Fellows.
Psychiatry and Disease in Children. 8.30 P.M. Dr. William Moodie and Dr. Reginald Miller: Enuresis.
THURSDAY.
Dermatology. 5 P.M. (Cases at 4 P.M.) Dr. H. W. Barber: 1. Hereditary Alopecia in Mother and Daughter. Dr. G. B. Dowling: 2. Congenital Developmental Abnormality. Dr. A. C. Roxburgh and Dr. R. Klaber: 3. Case for Diagnosis. Dr. Klaber: 4. Idiopathic Hypochromic Anæmia with Dermatitis Herpetiformis. Dr. Klaber and Dr. Freudenthal: 5–6. Blue Nævi (Jadassohn). Dr. G. Bamber: 7. Keratosis of the Nipples. Dr. G. Heggs: 8. Aplasia Phalangium. Dr. R. D. Moyle: 9. Cystic Hygroma with Recurrences in the Skin. Prof. L. J. Witts: 10. Dermatomyositis.
Urology. 8.30 P.M. Mr. O. L. Addison: Urology in Children.
FRIDAY.
Disease in Children. Cases will be shown at 4.30 P.M.
Epidemiology and State Medicine. 8.30 P.M. Dr. A. D. Gardner: Prophylaxis, Treatment, and Bacteriology of Pertussis.

MEDICO-LEGAL SOCIETY.
THURSDAY, April 23rd.—8.30 P.M. (Manson House, 26, Portland-place, W.). Prof. Laurie: The Application of Microscopic Methods to Deciding the History and Origin of Pictures.

CHELSEA CLINICAL SOCIETY.
TUESDAY, April 21st.—8.30 P.M. (Hotel Rembrandt, Thurloe-place, S.W.). Prof. J. A. Gunn and Dr. A. J. D. Cameron: The Trend of Modern Therapy.

PADDINGTON MEDICAL SOCIETY.
TUESDAY, April 21st.—9 P.M. (Great Western Royal Hotel Paddington, W.). Dr. Maurice Shaw: The Backward Bowel.

SOCIETY FOR THE STUDY OF INEBRIETY.
TUESDAY, April 21st.—4 P.M. (11, Chandos-street, W.). Annual General Meeting. Dr. J. D. Rolleston: On Snuff-taking.

ST. JOHN'S HOSPITAL DERMATOLOGICAL SOCIETY, 5, Lisle-street, W.C.
WEDNESDAY, April 22nd.—4.15 P.M., Clinical Cases. 5 P.M., Dr. George Bray: The Cutaneous Manifestations of Allergy.

LECTURES, ADDRESSES, DEMONSTRATIONS, &c.

UNIVERSITY OF BIRMINGHAM.
TUESDAY, April 21st.—3.30 P.M. (General Hospital), Mr. A. B. Danby: Recent Advances in the Diagnosis and Treatment of the Toxæmias of Pregnancy.
FRIDAY (Queen's Hospital), 3.30 P.M., Dr. J. F. Brailsford: The Possibilities of Antenatal Radiography in General Practice.

BRITISH POSTGRADUATE MEDICAL SCHOOL, Ducane-road, W.
MONDAY, April 20th—2.15 P.M., Dr. Duncan White: Radiological Demonstration.
TUESDAY.—2 P.M., Prof. E. H. Kettle: Pathological Lecture-demonstration. 3 P.M., Mr. E. J. King, Ph.D.: Phosphatase in Bone Formation and in Bone Disease.
WEDNESDAY.—Noon, clinical and pathological conference (medical). 2.30 P.M., clinical and pathological conference (surgical).
THURSDAY.—2.30 P.M., Dr. W. S. C. Copeman: Arthritis. 3 P.M., Dr. Chassar Moir: Operative Obstetrics.
FRIDAY.—2.15 P.M., Dr. A. A. Davis: Gynæcological Pathology. 3.30 P.M., Dr. Alan Moncrieff: Hygiene of the New-born Child. 5 P.M., Sir James Walton: The Surgical Aspects of Dyspepsia.
Daily, 10 A.M. to 4 P.M., medical clinics, surgical clinics or operations, obstetric and gynæcological clinics or operations, refresher course for general practitioners.

FELLOWSHIP OF MEDICINE AND POST-GRADUATE MEDICAL ASSOCIATION, 1, Wimpole-street, W.
MONDAY, April 20th, to SATURDAY, April 25th.—ROYAL EYE HOSPITAL, St. George's-circus, S.E. Afternoon course in ophthalmology.—ST. MARK'S HOSPITAL, City-road, E.C. All-day course in proctology. Courses are open only to members of the fellowship.

HOSPITAL FOR SICK CHILDREN, Great Ormond-street, W.C.
WEDNESDAY, April 22nd.—2 P.M., Mr. Denis Browne: Cleft Palate and Hare-lip. 3 P.M., Mr. H. C. Apperly: Irregularities of the Teeth and Jaws.
Out-patient clinics daily at 10 A.M. and ward visits at 2 P.M.

NATIONAL HOSPITAL FOR DISEASES OF THE HEART, Westmoreland-street, W.
TUESDAY, April 21st.—5.30 P.M., Dr. F. W. Price: Chronic Myocardial Disease.

MANCHESTER ROYAL INFIRMARY.
TUESDAY, April 21st.—4.15 P.M., Dr. F. E. Tylecote: The Physician and the Menopause.
FRIDAY.—4.15 P.M., Mr. John Morley: Demonstration of Surgical Cases.

GLASGOW POST-GRADUATE MEDICAL ASSOCIATION.
WEDNESDAY, April 22nd.—4.15 P.M. (Western Infirmary), Mr. J. Mill Renton: Toxic Goitre and its Treatment.

Appointments

ARMIT, ADAM, M.B. Edin., D.P.H., has been appointed Medical Officer for Chadderton.

BROWN, C. METCALFE, M.D. Glasg., D.P.H., Medical Officer of Health for Middlesbrough.

EDWARDS, L. M., M.D. Wales, Assistant Resident Medical Officer at the City of London Maternity Hospital.

GARLAND, H. G., M.D. Leeds, M.R.C.P. Lond., Consultant Assistant Physician to St. James's Hospital, Leeds.

HARTFALL, S. J., M.D. Leeds, M.R.C.P. Lond., Consultant Assistant Physician to St. James's Hospital, Leeds.

HUDSON, E. H., M.B. Camb., M.R.C.P. Lond., Hon. Assistant Physician to the West London Hospital.

KIMBELL, C. W., M.B. N.Z., Resident Medical Officer at the City of London Maternity Hospital.

MURRAY, D. S., M.B. Glasg., Assistant Pathologist to the West London Hospital.

ROBERTSON, MARGARET F., M.B. Leeds, Medical Officer to Maternity and Child Welfare for Middlesbrough.

WADE, C. H. T., M.B. Manch., D.P.H., Deputy Medical Superintendent, Baguley Sanatorium, near Altrincham.

Certifying Surgeons under the Factory and Workshop Acts: Dr. D. J. EVANS (Cowbridge District, Glamorgan); Dr. J. PRINGLE (Manchester South East District, Lancs.); Dr. W. R. MAXWELL (Rhondda (Porth) District, Glamorgan); Dr. G. R. GARDNER (Larkhall District, Lanarkshire).

Vacancies

For further information refer to the advertisement columns

Accrington, Victoria Hospital.—H.S. £150.

Altrincham General Hospital.—Jun. H.S. At rate of £120.

Ashton-under-Lyne District Infirmary.—H.S. At rate of £150.

Ayr County Council.—Asst. M.O. £500.

Birmingham, St. Chad's Hospital.—Jun. Res. M.O. At rate of £150.

Birmingham, Selly Oak Hospital.—Jun. M.O. At rate of £200.

Bradford Royal Infirmary.—Two H.S.'s. Each at rate of £135.

Bristol Eye Hospital.—Jun. Res. H.S. £100.

British Postgraduate Medical School, Ducane-road, W.—H.P.

Burnley Victoria Hospital.—H.P. At rate of £150.

Burton-on-Trent, Brelby Hall Orthopædic Hospital.—Res H.S. At rate of £150.

Cambridge, Addenbrooke's Hospital.—Res. Anæsthetist, &c. At rate of £130.

Canterbury, Kent and Canterbury Hospital.—H.S. At rate of £125.

Central London Throat, Nose, and Ear Hospital, Gray's Inn-road, W.C.—Hon. Assts. in Out-patient Dept.

Chester City Hospital.—Sen. Res. M.O. £400.

Coventry and Warwickshire Hospital.—Res. H.S. £125.

Doncaster, Royal Infirmary and Dispensary.—Res. Anæsthetist. Also H.S. Each at rate of £175.

Ealing, King Edward Memorial Hospital.—Sen. Res. M.O. At rate of £250.

Eastbourne, Princess Alice Memorial Hospital.—Psychologist.

Evelina Hospital for Sick Children, Southwark, S.E.—H.S. £120.

General Lying-in Hospital, York-road, Lambeth, S.E.—Jun. Res. M.O. and Anæsthetist. At rate of £100.

Hampstead General and N.W. London Hospital.—Physician to Out-patients.

Harrogate and District General Hospital.—H.S. At rate of £150.

Home Office, Whitehall, S.W.—Medical Inspector for Children's Branch. £738.

Hospital for Sick Children, Great Ormond-street, W.C.—Res. M.O. for Country Branch. At rate of £250. Also Surg. Reg. £200.

Hove General Hospital.—Res. M.O. At rate of £150.

Huddersfield Royal Infirmary.—Cas. O. £200. Also H.P. and Res. Anæsthetist. Also two H.S.'s. Each at rate of £150.

Hull, Beverley-road Institution.—Asst. M.O. £350.

Hull Royal Infirmary.—H.P. to Sutton Branch Hospital. At rate of £160. Also Second Cas. O. At rate of £150.

Ipswich, East Suffolk and Ipswich Hospital.—Cas. O. £168. Also H.S. £144.

Kidderminster and District General Hospital.—H.S. £150.

Lancashire Mental Deficiency Acts Committee.—Asst. M.O. £550.

Leicester, City General Hospital.—Res. M.O. At rate of £300.

Liverpool, Fazakerley Sanatorium.—Res. Asst. M.O. £200.

Liverpool, Ministry of Pensions Hospital, Mossley Hill.—Asst. M.O. At rate of £300.

Liverpool Sanatorium, Delamere Forest, Frodsham.—Second Asst. to Med. Supt. £200.

London Jewish Hospital, Stepney Green, E.—Res. M.O. and H.P. At rate of £150. Also H.S. and Cas. O. Each at rate of £100.

Macclesfield General Infirmary.—Second H.S. At rate of £150.

Manchester, Christie Hospital and Holt Radium Institute.—Asst. M.O. £400.

Manchester City P.H. Dept.—Asst. M.O.H. £700.

Manchester Royal Children's Hospital, Pendlebury.—Res. Surg. O. At rate of £125.

Manchester Royal Infirmary.—H.S. to Special Depts. At rate of £50.

Margate, Royal Sea-Bathing Hospital.—Asst. Med. Supt. £500.

Nottingham City Mental Hospital.—Jun. Asst. M.O. £350. Also Locum Tenens M.O. £7 7*s.* per week.

Nottingham General Dispensary.—Res. Surgeon. £250.

Oldham Royal Hospital.—H.S. for Special Depts. and H.P. At rate of £175.

Penshurst, Cassel Hospital for Functional Nervous Disorders, Swaylands.—Locum tenens. 10 guineas per week.

Plymouth City General Hospital.—Jun. Asst. M.O. £250.

Princess Beatrice Hospital, Earl's Court, S.W.—Res. M.O. At rate of £150.

Queen Mary's Hospital for the East End, Stratford, E.—Asst. Radiologist. £150.

Radcliffe-on-Trent, Notts. County Mental Hospital.—Second Asst. M.O. £459.

Rotherham Hospital.—H.P. £180.

Royal Chest Hospital, City-road, E.C.—Res. M.O. At rate of £150. Also H.P. At rate of £100.

Royal London Ophthalmic Hospital, City-road, E.C.—Two Out-patient Officers. Each £100.

Royal Naval Medical Service.—M.O.'s.

Royal Society, Burlington House, W.—E. Alan Johnston and Lawrence Research Fellowship in Medicine. £700.

Royal Waterloo Hospital for Children and Women, Waterloo-road, S.E.—Res. Cas. O. £150. Also H.P. At rate of £100.

Sheffield Children's Hospital.—H.S. At rate of £100.

Surrey County Council.—Jun. Asst. M.O. for County Sanatorium. At rate of £350.

Surrey Standing Joint Committee.—Part-time Pathologist and Medico-Legal Advisor to Surrey Constabulary. 100 guineas with extras.

Swansea County Borough.—Asst. M.O. £500.

Swansea General and Eye Hospital.—H.P. At rate of £150. Also Cas. O. At rate of £150–£175.

Taunton and Somerset Hospital.—H.S. At rate of £100.

Wolverhampton Royal Hospital.—H.P. At rate of £125.

The Chief Inspector of Factories announces vacancies for Certifying Factory Surgeons at Bruton (Somerset), Carlton (Notts), and Keswick (Cumberland). Latest date for receipt of applications April 21st.

Births, Marriages, and Deaths

BIRTHS

CALLENDER.—On April 6th, at Whitstable, Kent, the wife of Dr. T. A. R. Callender, of a daughter.

CAPPS.—On April 6th, the wife of F. C. W. Capps, F.R.C.S. Eng., Park-square East, N.W., of a daughter.

CUMMING.—On April 4th, the wife of Dr. John Cumming, of Hove, of a son.

EAGGER.—On April 2nd, the wife of Dr. A. A. Eagger, of Exeter, of a son.

FOWLER.—On April 7th, at Devonshire-place, the wife of Dr. Eric Fowler, of Crowborough, of a daughter.

HUDSON.—On April 11th, at Welbeck-street, the wife of Rupert Vaughan Hudson, F.R.C.S. Eng., of a daughter.

LEWIS.—On April 7th, the wife of Dr. Windsor Lewis, Cambridge, of a son.

NORRIS.—On April 2nd, at City-road, Finsbury-square, E.C., to Hélène Norris, M.D. Geneva, the wife of Donald C. Norris, M.D. Lond., F.R.C.S. Eng.—a son.

SINCLAIR.—On April 6th, at Lewes, the wife of C. Gordon Sinclair, F.R.C.S. Eng., of a son.

WOODD WALKER.—On April 13th, at Pembridge-crescent, the wife of Geoffrey Woodd Walker, F.R.C.S. Eng., of Queen Anne-street, W., of a son.

MARRIAGES

ASHTON—WOLFE.—At St. Clement Danes, London, on Feb. 29th, 1936, Eric G. Ashton, M.B., Ch.B. Dub., to Sylvia K. F. Wolfe, M.B., B.S. Lond.

LIST—CARR.—On April 4th, at Stone, Staffs, Dr. Howard Meredith List, to Elizabeth Maud, elder daughter of Mr. R. H. Carr, of Stone.

DEATHS

BINGLEY.—On April 10th, at Little Causey, Cranleigh, Ernest Horsford Bingley, M.R.C.S. Eng.

MITCHELL.—On April 12th, at Portsmouth, Arthur Martin Mitchell, M.D. Camb.

PAYNE.—On April 7th, at Leicester, Alfred Ernest Payne, M.B. Lond.

PRATT.—On April 11th, suddenly, at Morchard Bishop, Charles Claridge Pratt, L.M.S.S.A. Lond.

PRESTON.—On April 12th, at Mannings Heath, the residence of his sister-in-law, Joseph Charles Preston, L.D.S., of Brighton.

N.B.—A fee of 7s. 6d. is charged for the insertion of Notices of Births, Marriages, and Deaths.

HOSPITAL ACCOMMODATION FOR SOUTH MIDDLESEX AND RICHMOND.—The Minister of Health has sanctioned the raising of a loan of £96,650 by the South Middlesex and Richmond Joint Hospital Board for further accommodation in connexion with the treatment of infectious disease other than small-pox. The money is to be spent on erecting two new pavilion blocks, each containing 24 beds, and three cubicle blocks, each containing 12 beds, a new administration block, a nurses' home, and an operating theatre, together with a house for the medical superintendent and a lodge for the porter.